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THE RÔLE OF THE HÆMOLYTIC STREPTOCOCCI IN INFECTIVE DISEASE.

By C. C. Okell, *M.C.*, M.B. Camb., M.R.C.P. Lond.,
PROFESSOR OF BACTERIOLOGY IN THE UNIVERSITY OF LONDON, AND BACTERIOLOGIST TO UNIVERSITY COLLEGE HOSPITAL, LONDON.

II.—PROPERTIES OF ERYTHROGENIC (RASH-PRODUCING) TOXIN OF THE STREPTOCOCCI.*

The properties of the exotoxin of the hæmolytic streptococci which are responsible for the peculiar features of the scarlatinal exanthem and of the Dick test, are so important from the point of view of modern work on the prophylaxis of scarlet fever that no excuse need be offered for considering them in detail. One of the most remarkable properties of this toxin is that when it is suitably diluted and introduced into the human skin it produces a local erythematous patch which appears within a few hours, reaches a maximum within 24 hours and then rapidly fades away leaving at times a desquamating area but never signs of more severe tissue damage. The consistency and appearance of this local patch of erythema so closely resemble those of an actual area of rash in a subject with scarlet fever, that we readily infer that the mechanism of production in the two cases is identical. If this toxin is injected into susceptible human beings in large doses, for example in quantities upwards of a thousand times the dose used in the Dick test, a clinical condition results which resembles a self-limited attack of scarlet fever so closely that it has been described as "the scarlatinal syndrome" or in O'Brien's graphic phrase "miniature scarlet fever." The syndrome comes on a few hours after the injection. The patient often vomits, develops fever, a frequent pulse, a furred tongue, and a generalised rash which in appearance and distribution is indistinguishable from that of scarlet fever. An interesting symptom recorded by a number of observers is soreness of the throat. As in true scarlet fever the rash avoids the face, and the appearance of circumoral pallor has been recorded. A slight albuminuria is common and there may even be transient hæmaturia. Recovery even from large doses is apparently rapid and complete. Toyoda, Moriwaki, and Futagi [1] have recorded a case of the scarlatinal syndrome in which desquamation followed.

No experimental animal has so far been discovered which may be compared with man in susceptibility to this toxin, and thus we have been denied those methods of study which have yielded such a rich harvest in the study of diphtheria. It is doubtful if an intradermic reaction strictly comparable with the Dick reaction can be obtained in any animal other than man. I have attempted to produce Dick reactions in horses, cows, sheep, goats, dogs, cats, ferrets, rabbits, guinea-pigs, rats, mice, and hens but always ineffectually. Even monkeys, at least those of the *rhesus* family, have, in my experience, no skin susceptibility to doses of toxin a hundred times greater than that used for the Dick test in human beings.

Kirkbride and Wheeler [2] claim to have obtained reactions comparable with Dick reactions on the skin of Saanen goats. Their method has been used on a considerable scale at the New York State Department of Health for purposes of standardising streptococcal toxins and antitoxins. Other workers seem to have had very little fortune in confirming these observations of the Albany workers. This may, of course, be due to a failure to secure properly susceptible goats. My own experiences with such goats as I could procure were entirely disappointing. Certain peculiar skin reactions were observed, but these appeared to be unrelated to the specific toxic reaction of the toxin nor could I obtain any results which were capable of numerical interpretation. Ando states that the skin of white pigs will give a Dick reaction; but some dozen pigs, young and old, which I examined failed to give anything resembling a Dick reaction, even when large amounts of toxin were injected. This, I believe, has been the experience of many other workers who have attempted to confirm Ando's observations.

As Parish and I [3] showed, the rabbit, while it gives no skin reaction, is susceptible to large intravenous doses of erythrogenic toxin. In 96 per cent. of cases the animals died within six days, usually within 48 hours. When, however an, adequate dose of streptococcal antitoxin was previously given 87 per cent. of the rabbits survived for longer than six days. In our earlier experiments it needed 5 c.cm. or more of the strongest toxin we could obtain to cause death in this way. The dose employed was at least 5000 times that required to produce a typical Dick reaction, and 50 times that required to produce a generalised scarlatiniform rash, in a susceptible human subject. Hartley [4] and also Pulvertaft [5] with much smaller volumes of concentrated toxin subsequently obtained similar lethal effects and similar specific neutralisation with antitoxin. Hartley produced death with as small an intravenous dose as 0·2 c.cm. of his highly purified preparations. Pulvertaft describes in some detail the gross and minute anatomical changes found in rabbits dying from intravenous injections of toxin, but it is difficult to say if these are in any way characteristic. I was personally unable to satisfy myself that the gross post-mortem changes which were found in such animals gave any reliable information bearing on the essential toxological properties of streptococcal filtrates. Pulvertaft states that the kidneys of these rabbits showed "degeneration of tubules with great congestion in glomeruli and tubules," and that in rabbits which survived more than five days sections showed "cellular casts in the tubules and evidence of round-celled proliferation around the glomeruli."

It has often been surmised that nephritis, a justly feared sequel of scarlet fever and indeed of all streptococcal infection, can be ascribed to the action of the erythrogenic toxin. It has been mentioned that transient albuminuria and even hæmaturia may follow the injection of the sterile toxin into human beings, but it is to be noted that these symptoms accompany the rash at its height and rapidly disappear with the rash, while the characteristic feature of scarlatinal and streptococcal nephritis generally, is that it makes its appearance after a considerable latent period, often after all the acute manifestations of disease have passed away. Two further points may be referred to suggesting that the erythrogenic toxin is not the cause of nephritis. Nephritis may follow in cases of scarlet fever with very slight rash and cases of streptococcal infection with no signs of rash at all, nor has treatment with streptococcal antitoxin ever been clearly proved to influence the subsequent incidence of nephritis.

A little can be learnt about the properties of the erythrogenic toxin from observations of its effects upon the human skin. The toxin, whether injected

* The Second Milroy lecture for 1932, delivered before the Royal College of Physicians of London on Feb. 23rd.

intradermically as in the Dick test or pricked into the skin as in Lewis's [6 7] technique, produces in susceptible persons a patch of bright scarlatiniform erythema. Serious damage of the skin does not take place even when very large doses are injected. Large doses may produce extensive areas of reaction and even a more intense erythema, but, except for occasional minute petechiæ which seem to be due to the bursting of over-distended vessels, nothing resembling a tissue necrosis is to be observed. It is not in fact a pyogenic toxin.

Little can be said of the nature of the erythematous reaction. It is at least different from the reaction to trauma or to the histamine-like effect described fully by Thomas Lewis. It is perhaps most analogous with the delayed erythematous reaction produced by exposure to a moderate dose of light as has been described by Lewis and Grant. We do not in fact know whether or not the cutaneous manifestations are in the main due to a direct action of the toxin on the vessels or indirectly through the nervous system.

A SINGLE ERYTHROGENIC TOXIN?

A majority of hæmolytic streptococci from acute human disease produce one and the same erythrogenic toxin; this conclusion follows from the observations on human beings by McLachlan,[8] J. Smith,[9] Kirkbride and Wheeler,[10] Toyoda [1] and his colleagues and ourselves. It also obtains support from experiments on animals. Not only do hæmolytic streptococci from diverse forms of disease produce a similar septicæmia in rabbits but so far as Parish and I [3] could ascertain the lethal effect of different streptococci introduced intravenously could be specifically modified by the use of antitoxin prepared against filtrates from puerperal fever, erysipelas, and cellulitis, as well as scarlet fever strains. We recorded similar cross-neutralisation using filtrates (toxins) for the intravenous injection.

It would take too long to review in full the evidence in favour of there being one type of erythrogenic toxin among the hæmolytic streptococci. Some of the claims made in favour of a plurality of toxins are based on quantitative differences in effects and as I shall endeavour to show later, quantitative ideas must be applied to the study of this type of toxin with a due appreciation of their limitations. The immunological identification of toxins is, however, a sufficiently precise science and it seems to me a reasonable attitude to be chary of mere statements on the subject. If there are in fact other streptococcal toxins it should be possible to hand them over in bottles for impartial study. A toxin which cannot stand this acid test hardly calls for recognition.

From this general statement we may have possibly to exclude the hæmolytic *Streptococcus epidemicus* which has of late been found repeatedly in connexion with milk-borne epidemics of sore-throat, particularly in America. Except in its greater tendency to produce capsulated forms this streptococcus differs little from the typical pyogenic streptococci, of which it may be merely a colony variant, but Pilot and Dreyer [11] have recently claimed that it forms an erythrogenic toxin similar in toxic properties to that of scarlet fever strains but immunologically distinct from it. Nor is it improbable that with the advance of research further erythrogenic toxins with special immunological features will be separated out from streptococci. But so far as current knowledge goes, with the possible exception of the case of *S. epidemicus*, it may be stated that only one immunologically distinct erythrogenic toxin has been identified in connexion with the hæmolytic streptococci.† In my experience very few strains of hæmolytic streptococci, whatever their source, are met with that fail to produce this toxin to a greater or less extent under laboratory conditions. It seems to be the rule that strains from scarlet fever produce the toxin much more actively than strains from ordinary streptococcal conditions without rash, but to this rule there are many exceptions. Strains from typical scarlet fever are sufficiently commonly found that produce toxin poorly in the laboratory and I have met with strains from ordinary streptococcal angina and from erysipelas which have in-vitro toxigenic powers comparable to typical scarlet fever strains.

The production of the erythrogenic exotoxin appears to be a direct function of the growth and multiplication of the streptococci. Observations made by Watson and myself in 1924 (unpublished) indicate that the curve of toxin production shown by Dochez's streptococcus follows closely the curve of growth of the cocci during the logarithmic phase. On Hartley and Watson's modification of Douglas's trypsinised broth, maximum growth was reached within 16 to 24 hours, by which time a maximum of toxin is reached. If the pH of the broth at the time of inoculation is pH8 at the end of the growth phase it reaches pH5 to 6 and thus the pH change can be used for judging the best time to harvest the toxin.

Immunological Properties of the Erythrogenic Toxin.

It is no exaggeration to say that the discovery by G. F. and G. H. Dick in 1924 of a skin test which was closely correlated with immunity to scarlet fever inaugurated a new era in the study of streptococcal disease. The new test looked as if it would at once emulate the Schick test in its theoretical interest and in its practical application. The codified knowledge which had accumulated in connexion with the Schick test seemed to be immediately applicable to the Dick test. These hopes have been, however, to a large extent disappointed. Difficulties, both practical and theoretical, were almost at once met with which indicated that our understanding of this test and its application was on a much more insecure basis than our understanding of the analogous Schick test. This unsatisfactory position is, to a great extent, due to the absence of a suitable experimental animal for the purposes of laboratory investigation. To an almost equal extent it is due to certain peculiar features of the erythrogenic toxin. The contribution of the Schick test to the elucidation of the immunological problems of diphtheria is due to the fact that the test lends itself to quantitative study. Its value in this respect depends in turn on the great precision with which diphtheria toxin and antitoxin can be measured on small laboratory animals. By Römer's intradermal technique as perfected by Glenny [12] it is possible to detect as small a quantity of diphtheria toxin as one-thousandth of the minimum lethal dose (M.L.D.) for a guinea-pig and toxins can be compared with a percentage error of about 5 per cent. Now it has proved impossible to measure streptococcal toxin in the same manner even in susceptible human patients.

If, for example, one attempts to compare the effects of a toxin dilution of a certain strength with those of a dilution a quarter of that strength, extremely discordant results may be obtained if only a small number of susceptible subjects are used. Parish and I found that using 0·2 c.cm. of two dilutions of one toxin (1/2000 and 1/4000) in the Dick test

† Williams and Gurley (Jour. Bact., 1932, xxiii., 241) have, however, found that the toxin from the so-called *S. epidemicus* is immunologically identical with that from scarlatinal strains. These authors do not consider *S. epidemicus* constitutes a separate species

we only found the Dick reaction with 1/2000 greater than that with 1/4000 in 72 per cent. of a large group of individuals. We were thus only able to distinguish a toxin dilution from one twice its strength or half its strength on a strictly statistical basis. On a few subjects the chance of a correct comparison was little better than 1 in 2.

Nor does any alternative method of titration present itself which gives greater accuracy. Whether we compare toxins on normal individuals, early cases of scarlet fever, scarlet fever convalescents, or by intravenous injection of the rabbit, whether we assess the values by comparison of individual Dick reactions on the same patient or on different patients, or whether we rely on comparisons of the Dick-positive rate of a large group of individuals, normal or convalescent, we have not been able in our own work to do more than distinguish a toxin amount x from an amount $2x$.

Similarly, in an investigation into the limits of accuracy of the titration of streptococcal antitoxin we were unable by skin neutralisation tests, Schultz-Charlton tests, or passive immunity results on human beings, or by the rabbit method, to do more than distinguish an antitoxin amount x from one $2x$. Compare this with the beautiful precision achieved in titrating the analogous diphtherial product, in which 1/20 differences of antitoxin strength can be readily detected by intradermic tests on guinea-pigs and the presence of so small a quantity as 1–20,000 unit of antitoxin in a 0·1 c.cm. volume be detected (Glenny) under good experimental conditions.

The failure to discover a metrical method providing a degree of accuracy adequate for the purposes of investigation and the confusion that has resulted therefrom illustrate only too well the truth of Clerk Maxwell's remark that "the most important step in the progress of every science is the measurement of quantities." It is this failure in quantitative methods, combined with a very prevalent lack of appreciation of the serious nature of the impasse reached, which has perhaps more than anything else kept our knowledge of the Dick test in relationship to human immunity so confused and unsatisfactory. It must be recognised that to the present moment it has proved impossible to match two successive batches of toxin for the Dick test so closely that they will give approximately the same results on a large series of human beings. It is fortunate that in Great Britain nearly all the routine tests recorded since the test was introduced in 1924 have been done with one batch of toxin which has been under constant supervision as regards stability and other properties. This means that in England at least, the Dick tests which are recorded are numerically comparable. But it is difficult to link up the work done elsewhere with that done in our own country, and much of the experience accumulated on the Dick test is thus not negotiable between nation and nation nor in many cases between individual and individual.

FURTHER DIFFICULTIES.

In addition to the difficulties and uncertainties of the test which depend upon difficulties of titration of toxin and antitoxin, there are other directions in which the Dick test falls short of the Schick test as a weapon in the control of disease. It must be admitted that many careful observers have met with scarlet fever in clearly Dick-negative individuals. Cases of this kind, in which the prediction of immunity as judged by skin-test observations is falsified, occur of course also in connexion with diphtheria, but so far as one can say very much less frequently. On the other hand the presence of a Dick-positive reaction does not appear to be a clear indication of susceptibility to scarlet fever. It is true that those obviously immune to the disease, such as the more seasoned physicians and nursing attendants at fever hospitals, are almost invariably Dick-negative whether they are known to have had scarlet fever or not, but as we pointed out some years ago,[13] a large proportion of persons who have had a history of scarlet fever in early life are still positive to the Dick test read in the ordinary way (13, or 65 per cent. in one group of 20). In some cases the reaction shows a diminution in size but in others it is frankly positive. Yet clinical experience indicates how rarely scarlet fever is met with in persons with a history of previous infection and one can hardly suppose that more than a fraction of these Dick-positive persons would in reality contract the disease if exposed to it.

Most observers have failed to record anything approaching a hundred per cent. Dick-positive rate during the first one or two days of the disease, and we cannot explain this away by assuming that patients may change from a positive to a negative reaction in this time. All our knowledge suggests that a distinctly longer interval must elapse before we can expect the development of immunity to show itself in cases of scarlet fever.

One also meets with an unexpected number of Dick-positive individuals during convalescence from scarlet fever even when there is little doubt as to the correctness of the diagnosis. It one series of 119 cases we found as many as 22 Dick-positive between the third and the twelfth week after onset, 12 being apparently fully positive. In 14 at least out of the 22 cases no reason whatever could be found to doubt the clinical diagnosis.

That patients may pass through a definite attack of scarlet fever yet remain Dick-positive may have a bearing on the subject of relapses. One at least of those mentioned who had passed through a clinically definite attack and had remained Dick-positive developed a second and typical attack a day after the Dick test had been read. The alternative explanation of relapses—that they are due to a second invasion with a streptococcus of a different agglutination group from the first—is inadmissible since, as I have already pointed out, there is no evidence that the different serological groups of streptococci produce more than one erythrogenic toxin, and if a negative Dick test is in reality a useful indication of true immunity there is no reason against inferring that a Dick-negative convalescent should not be as immune to the new as to the original invader. Apart from other evidence, the rareness of second attacks of scarlet fever supports strongly the view that the erythrogenic toxins of the streptococci obtained from cases of the disease are identical.

These points illustrate, I think, sufficiently clearly the intrinsic difficulty of estimating the value of the Dick test as a practical measure in preventive medicine. To say that the discrepancies that one meets with depend upon a bad choice of the test dose of toxin simply emphasises the fundamental difficulty caused by there being no true standard of measurement in these matters; one observer can only argue with another when both have used the same toxin in the same dilution. Even then the discrepancies remain.

PSEUDO-REACTIONS.

Ando and Kurauchi [14] and Toyoda have attempted to account for the admitted difficulties in Dick-testing by suggesting that an adventitious nucleo-protein derived from the bacterial bodies is present in the crude erythrogenic toxin and that discrepancies may disappear if a purified toxin is used. They

would, in fact, ascribe much of the difficulty to the occurrence of "pseudo-reactions." The importance of pseudo-reactions in interpreting the findings of the Dick test seems to be exaggerated by Ando. The toxins which have been extensively used in recent years only give rise to pseudo-reactions, in the dilution used, in very exceptional cases. In many hundreds of consecutive Dick tests I have failed to meet with any reaction that I could ascribe to the "heat stable" substances to which Ando applies the rather misleading term "endotoxin." That this is common experience is indicated by the fact that many workers have given up the use of a control injection in practical routine.

Compared with the exotoxins of the diphtheria, tetanus, and gas-gangrene bacilli the erythrogenic toxin of the hæmolytic streptococcus is a remarkably stable reagent. Its keeping properties and its stability to heat are so superior to those of the classical toxins that it has often been suggested that it should not lightly be classed with them. Dilutions of a toxin in saline are practically uninfluenced by heating for ten minutes at 75° C., an exposure which almost always completely inactivates diluted diphtheria toxin. It is now generally recognised that in order to destroy all the toxin in a 1/1000 dilution of a typical active filtrate it is necessary to heat it for at least two hours at 95–100° C., an exposure which of course makes it difficult to assess the significance of pseudo-reactions, since any coagulable protein must be severely damaged by such treatment.

While the stability of the toxin has been a very helpful property in the issue of materials for the Dick test, in one direction it has caused difficulty. In the method of active immunisation against scarlet fever by means of the toxin we have to face the fact that to protect children against a disease which at the present time causes little terror we have to employ a troublesome and often disturbing method of immunisation. To avoid all untoward effects of immunisation it is necessary to advance slowly and cautiously from dose to dose of toxin. If, on the other hand, a rapid immunity is required from a practical number of injections it appears impossible to avoid a certain percentage of local and systemic reactions and, speaking generally, the results have not been considered by most hygienists to be worth the cost. There is in fact no comparison between diphtheria and scarlet fever prophylaxis in the ease and safety of the immunising process or the certainty of the practical result.

A SCARLET FEVER TOXOID?

Much of the confidence which has been put in the safety of immunisation against diphtheria in recent years comes from the use of toxoid in one form or another as the prophylactic agent, and the question arises whether a similar modification of scarlet fever toxin exists. By a toxoid we mean a derivative of a toxin which, while it preserves the specific antigenicity and combining power of the original toxin, lacks its toxic properties. Ehrlich recognised the existence of material with such properties in aged toxins, but the discovery of Löwenstein that the classical exotoxins could be simply converted into toxoid by exposure to formalin made it possible to control the production of toxoid at will. Ramon's discovery of an in-vitro method of measuring toxoid (and thus indirectly antigenic power) made it still further possible to extend the use of toxoid in practical immunisation against the common exotoxins.

It is unnecessary to say that following the introduction of toxin immunisation against scarlet fever, efforts were made by many workers to produce a formol-toxoid from the active toxin. It was found that the remarkable stability of the toxin against heat was paralleled by its stability when treated with formalin. When 0·3 per cent. formalin, the amount usually used for "toxoiding" diphtheria toxin, was added to the streptococcal toxin, little change was noted even when kept for many weeks at 37° C. By increasing the amount of formalin to 0·5 per cent. or more and keeping for several weeks, a considerable loss of toxicity took place.

It is doubtful if any formal proof exists that a change from streptococcal toxin to toxoid takes place under these conditions of detoxication, and so far as I can ascertain immunisation has never been obtained by such material unless at least 1/100 of the original toxic activity is retained.

Veldee [15] obtained a 96·9 per cent. Dick-negative rate when immunising Dick-positive adults and children with a formalinised toxin retaining only a 1/100 of its original toxicity as estimated by skin tests. He gave three to five doses of the material usually with an interval of 21 days between doses. The total quantity of active toxin given was less than the equivalent of 2000 skin test doses, yet it is not impossible that so small an amount of active toxin given with such long intervals between doses might account for the resulting immunity.

It also appears from Toyoda, Moriwaki, and Futagi's [1] observations on "toxoid" immunisation that toxic and antigenic power disappear pari passu in the formalinisation process. A significant immunity was only obtained when the material retained some degree of toxicity and the best all-round results were obtained with a preparation that produced generalised rashes in 1·3 per cent. of individuals immunised.

Other methods of study have equally given very uncertain indications as to the existence of a true toxoid to the streptococcal toxin. I have myself on many occasions attempted to utilise the flocculation test for the examination of this question and always without results. Eagles [16] was similarly unable to convince himself that such a test has any value, though Ramon [17] and his colleagues have claimed that the combining power of streptococcal toxin and antitoxin can be estimated in this way. Certain phenomena met with in the study of neutralising effects in human beings, particularly in those individuals who have a certain degree of immunity, might be interpreted as depending upon the presence of a combining as apart from a toxic element, but the difficulty of metrical precision in the estimations of such effects makes it unsafe to force their interpretation. It thus seems that we must prove the existence of a "scarlet fever toxoid" before discussing its use.

In dwelling on the disadvantages and difficulties I do not wish to imply that the methods of Dick-testing and active immunisation against scarlet fever have not an important place in preventive medicine. Already the incidence of scarlet fever among the nursing staffs of an increasing number of isolation hospitals has been reduced to negligible figures and the recent work of Stallybrass [18] indicates that practical results may even be obtained in children's institutions.

The "Allergic" Conception of Scarlet Fever.

A point of great biological interest which has arisen in the study of the Dick test is the curious lack of reactivity to the test observed in children during the first few months of life. With the exception of a series of interesting papers by Jean Cooke [19] there has been little comprehensive work carried out on this subject. Cooke showed that the majority of new-born children are not skin-sensitive to considerable amounts of the erythrogenic toxin. The lack of

sensitiveness was proved not to be due to the presence of antitoxin derived from the mother for not only had many Dick-positive mothers children who were Dick-negative, but the Dick-negative children had no detectable antitoxin in their blood. As the child grows older, skin-sensitiveness to the toxin gradually develops, so that at the end of the first year of life nearly all children have become sensitive and give a positive Dick reaction. Cooke connects the development of sensitiveness with the common presence of hæmolytic streptococci in the respiratory passages of infants.

In support of this view he states that infants more or less isolated from each other developed sensitiveness more slowly than those grouped together in residential institutions. In a group of 100 children under ordinary domestic conditions only one was found to harbour hæmolytic streptococci, while in a group of 100 who were in a foundling home 64 harboured such streptococci. Sensitiveness to toxin was found to develop earlier and more markedly in the latter group.

He also claims that in one instance an insensitive child was made sensitive by the injection of serum from a very sensitive person, in other words, the sensitiveness could be passively acquired. These observations Cooke has used to support the theory that the acquisition of sensitiveness to streptococcal toxin is an anaphylactic type of phenomenon, a theory which from time to time has had many adherents in the past and is indeed a component in the outlook of many modern workers on scarlet fever.

Dochez and Sherman,[20] on the basis partly of human observation and partly on animal experiments, come to very much the same view. They found that while guinea-pigs are normally insensitive to intracutaneous injections of filtrates from toxigenic streptococci, the animals could to some extent be made sensitive by previous injection with cultures and filtrates. They have even described a generalised erythema following the injection of a sensitised guinea-pig.

In our own experiments we were quite unsuccessful in sensitising guinea-pigs and rabbits to toxin as such. It was comparatively easy to reproduce Dochez and Sherman's phenomenon in guinea-pigs, but we found that in "sensitised" animals, skin reactions could be elicited not only by the injection of active scarlatinal toxin but also with filtrates heated to 100° C. for three hours, an exposure which we have found destroys all potency in a toxin as judged by reactions in Dick-positive human beings. Nor could these reactions be prevented by mixing the toxin with potent antitoxin. The sensitisation was evidently against some streptococcal protein not against the toxin as such. Mackie and McLachlan [21] have come to a similar conclusion as to the nature of the Dochez-Sherman phenomenon.

The so-called anaphylactic or "allergic" conception of scarlet fever has to my mind little to recommend it. The phenomenon presented by scarlet fever has no sufficiently close resemblance to properly defined anaphylactic reactions or to such peculiar reactions as the tuberculin reaction to provide a basis for a useful analogy. Allergy is a term used too often in ætiological arguments to give a touch of mystification to ignorance. So far as current knowledge goes we cannot readily identify "immunisation" with "desensitisation," nor anaphylactic antibodies with antitoxins.

The skin insusceptibility of infants to streptococcal toxin is by no means an isolated phenomenon in the immunology of toxins. It is for example well known that a majority of children under six months of age are Schick-negative and that only between the ages of 4 to 8 months do they become susceptible to the Schick dose of toxin. This has been ascribed to the passive transference of diphtheria antitoxin from mother to child via the placenta, which is known to take place from the work of Gröer and Kassowitz.[22] The explanation of the rather long duration of the passive immunity thus conferred was that the antitoxin was in the form of homologous or maternal protein and would be much longer retained than it would have been had it been conferred in the form of a heterologous protein such as antitoxin derived from the horse. It is true that passive immunity is conferred to the child by those mothers who have antitoxin in their blood, but it by no means follows that such small quantities of antitoxin as are found in newborn children would last sufficiently long to account for the large number of children in the third and fourth month who are still Schick-negative. Glenny, Maizells, and myself have recently taken up the investigation of this subject and we have found that out of 37 children between the ages of 3 weeks and 6 months only two were Schick-positive, 29 out of the 35 Schick-negative children had less than 1/500 unit of antitoxin per c.cm. of blood and 21 had 1/1000 unit or less. The failure of small children to react to the Schick test is not therefore necessarily associated with the presence of circulating antitoxin. The problem of insusceptibility of infants to the Dick test has thus its parallel in the Schick test. We have not yet data which allow us to decide whether or not this non-reactivity of the skin is associated with a general insusceptibility to the toxin, but epidemiological experience strongly suggests that very small children show a remarkable immunity to both diphtherial and scarlatinal infection. If this is really so it is a strange provision of nature that after birth we actually *develop* a susceptibility to diphtheria and scarlet fever. It would be premature to attempt to explain how children acquire sensitiveness to bacteria in this way. Hæmolytic streptococci are certainly sufficiently widespread that their presence could be invoked to explain a specifically acquired sensitiveness to them and their toxin, but our experience does not allow us to admit that toxigenic diphtheria bacilli are similarly ubiquitous and could account for the universal acquirement of sensitiveness to diphtheria toxin during those first and usually sheltered months of infant life.

In this connexion I might refer to some observations of Parish and myself [23] on streptococcal infections in rabbits. We found that young rabbits are significantly less sensitive to intravenous injections of living hæmolytic streptococci and also to their toxic filtrates than rabbits of greater age, and we were unable to increase their sensitiveness by artificial methods.

The problem of the acquirement of susceptibility to certain infecting agents and their toxins is a very interesting one and calls for more thorough investigation, but lightly to accept explanations of scarlet fever on the ground of "allergy" would be to constitute an ill-advised revolutionary change in our immunological ideas. It is perhaps simpler to restate the problem in Erhlich's terms and consider that at an early stage of life certain "receptors" have not yet been developed; this is not only indicated by the fact that the cells cannot be poisoned but also, if we accept Grasset's [24] observations on the failure of chicks in the egg to develop antibodies to diphtheria toxoid, by their lack of antigenic response as well.

Desquamation.

Before leaving the subject of the erythrogenic toxin of the streptococci there is one problem which is, I think, worth referring to. It is a time-honoured clinical custom to accept the appearance of desquamation as clinching the diagnosis in a difficult case of scarlet fever. I have already mentioned that Toyoda records desquamation as following an overdose of the sterile erythrogenic toxin of the streptococcus and indeed it is difficult to avoid the

view that desquamation is a direct result of the skin injury sustained at the time rash is florid. While it may be admitted in a majority of cases to be a *petitio principii* to diagnose scarlet fever from desquamation alone, many experienced observers claim to have seen desquamation following disease without any rash having been noted, and these cases have often been found to propagate fresh cases of typical scarlet fever. The difficulty is well expressed by Graves [25] in his Clinical Lectures.

"We are taught," he says, "to look upon desquamation as a result of cutaneous affections of an inflammatory character; and it is an opinion, very generally maintained, that in scarlatina, as in psoriasis, the peeling off of the cuticle depends on the peculiar state of the skin produced by inflammation." In the same lecture he quotes the case of a young lady with sore-throat and fever who desquamated and in whom, though he had her under constant observation, he nevertheless failed to observe a scarlet rash at any time during the disease. He adds that three members of the household subsequently contracted typical scarlet fever and that the lady's father developed sore-throat.

Now that a rash-producing toxin has been isolated from the causal agent of scarlet fever, the problem raised by Graves becomes none the less difficult. It is hard to imagine that desquamation really follows cases without a rash and it is always possible that in some cases the rash may be evanescent, perhaps nocturnal, and thus be missed. The Dick test may provide a method which may throw some light on the matter and it would be interesting to know whether such desquamating cases of "scarlet fever" without apparent eruption are usually positive or negative to the test and, if positive, whether the reaction becomes negative during the course of the disease.

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WORCESTER INFIRMARY.—The "record" number of 2141 in-patients was received last year; their average stay was 19·5 days, and their average cost 6*s.* 7½*d.* per day. At £120 18*s.* 7*d.* the cost per occupied bed showed a reduction of £7. Out-patients, of whom there were 6369, cost 10*s.* 3½*d.* each. The hospital is being extended at a cost of £60,000, little more than half of which has yet been obtained.

THE EFFECTS OF INJURY UPON THE BRAIN.*

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THE effects of direct injury to the brain, as considered by the neurologist, fall naturally into two groups. The one comprises those cases which end fatally, usually within the first two or three days, with evidence post mortem of gross laceration and contusion. Cases within this group provide little opportunity for clinical study. From the moment of injury to that of death the clinical state is that of profound stupor. The second group, comprising all those patients who survive the injury, offers a field of neurological inquiry which is as fascinating as it is difficult. It is from this clinical field that I shall select certain problems for discussion.

Traumatic Stupor.

The first is that afforded by the condition which I shall designate "traumatic stupor." I have chosen this term deliberately, even though it adds to the plethora of labels. It seems to me that we need some such title, clinical and descriptive, and therefore of lasting value, to cover the major effects of cerebral injury.

That a patient is suffering from traumatic stupor is a simple statement of fact, as a rule easily determined. Whether he is suffering from cerebral contusion or cerebral œdema or the after-effects of "concussion" is a question at present unsolved. Traumatic stupor, therefore, I take, in its several degrees, to cover all those conditions in which, after recovery from the initial and complete loss, consciousness remains clouded. In its severe degree the clinical picture is one with which we are familiar in hospital experience. I shall not attempt to describe it in detail, but would draw attention to three of its most striking features:—

1. The mental state varies from that of profound stupor to a moderate clouding of consciousness, with phases of irritability, excitement, and delirium.
2. In the great majority of cases signs of focal damage to the brain are conspicuously absent.
3. In relation to the severity of the mental disturbance in the earlier stages recovery of cerebral function is remarkably rapid and complete.†

PATHOLOGY.

For the proper treatment of this condition we need a true estimate of its pathological basis. But direct evidence of this is, for the most part, lacking. We have therefore to depend largely upon a comparison of the clinical picture with analogous states of other causation, together with such information as may be derived from our knowledge of intracranial physiology and the disturbances of function likely to result therein from trauma.

In order to explain the association of a profound disturbance of the mental state with absence of localising signs and a relatively rapid and complete recovery, we look for a widespread or diffuse pathology. An explanation which at first sight appears acceptable is that of a general embarrassment of the capillary circulation from increased intracranial pressure, the result of multiple hæmorrhages and œdema. This

* Based upon a paper read at the International Neurological Congress, Berne, 1931.

† As judged by our somewhat coarse tests.

view has been most ably expounded by Trotter. I shall, however, put forward certain objections to the acceptance of the hypothesis that increased intracranial pressure is the essential cause of the clinical state we are considering.

In the first place the clinical picture of traumatic stupor is not strictly comparable with that encountered in patients whose cerebral symptoms are known to depend upon increased pressure. In a case of hydrocephalus, for instance, caused by a subtentorial tumour, the mental state is, as a rule, that of stupor with apathy. There is usually none of that irritability, restlessness, and confusional excitement which characterise the state which I have called traumatic stupor and which have earned for it such descriptive titles as "cerebral irritation" or "traumatic delirium." Indeed, if we look for comparable clinical states, we shall find them in such conditions as infective or toxic delirium, or in encephalitis, rather than in simple states of increased intracranial pressure.

The second important objection is that, although in the majority of cases of traumatic stupor the pressure of the cerebro-spinal fluid is raised, I have found no correlation between the degree of pressure and the severity of the clinical state, and in some instances of severe traumatic stupor have found the pressure little raised or even normal. For example:—

A man, aged 66, was knocked down by a car on the night of June 30th, 1929, and admitted to hospital late the same night. On admission he was in a state of stupor. I saw him on July 2nd, 36 hours after the injury. There were abrasions of face and scalp, but no evidence of fractured skull. He was stuporose and restless, needing to be restrained at times from getting out of bed. I could find no signs of any focal lesion of the brain. Both plantar responses were flexor. The cerebro-spinal fluid showed a pressure of 120 mm. of water, and was evenly blood-stained. During the subsequent ten days he remained so confused and restless as to need a male attendant. He gradually recovered, and when last seen, five months later, was quite well save for occasional giddiness on turning his head quickly.

Comparable observations are:—

Male, 52. Nine days after injury: stupor continuous since accident; cerebro-spinal fluid xanthochromic; pressure 130 mm. water.

Female, 46. Five days after injury: restless stupor; cerebro-spinal fluid slightly blood-stained; pressure 150 mm. water.

Male, 48. Two days after injury: stuporose; cerebro-spinal fluid slightly yellow; pressure 110 mm. water.

Male, 16. Three days after injury: semi-conscious and resistive; cerebro-spinal fluid clear, but contained many red cells when examined microscopically; pressure not above 170 mm. water, despite struggling during the reading.

I submit, therefore, that increased intracranial pressure from œdema and hæmorrhage cannot be the essential cause of traumatic stupor.

An alternative hypothesis which has been ably supported by Bagley, both from clinical observation and animal experiment, is that subarachnoid hæmorrhage may play an important part in the causation of symptoms. I have found, however, that there is no constant relation between the amount of blood in the cerebro-spinal fluid and the severity of the clinical symptoms. The cases which I have already quoted illustrate this point.

We must therefore, I believe, look for some other explanation. Direct pathological evidence is scanty but suggestive. Careful microscopical examination in cases proving fatal within the first few days, without compound fracture of the skull or compression from meningeal hæmorrhage, shows, in addition to scattered hæmorrhages, widespread alterations in the structure of nerve-cells and fibres. Similar examination, when it has occasionally been possible at a later date in cases that have survived the injury and died of intercurrent disease, has shown chromatolysis and lipoid degeneration of nerve-cells, fragmentation and fatty degeneration of myelin, and a widespread and diffuse reactive process of the micro- and macro-glia (Rosenhagen). These changes, which Rosenhagen well describes, are to be found in the form of multiple small foci throughout the cerebral cortex in its whole extent.

I am led, therefore, to the conclusion that the essential cause of traumatic stupor is direct injury to the neural tissues with subsequent reactive changes, and that increased intracranial pressure and subarachnoid hæmorrhage play a subordinate rôle.

TREATMENT.

This conclusion, if valid, will have an important bearing upon treatment. In every case of traumatic stupor lumbar puncture should be performed, and the manometer should be employed. If the spinal fluid pressure is found to be high, it should be reduced by drainage to a normal level, and further treatment, such as concentrated magnesium sulphate solution per rectum or hypertonic glucose solution intravenously, should be given to reduce intracranial pressure. Lumbar puncture in such a case should be repeated if necessary, so that the result of treatment may be followed. A heavily blood-stained fluid provides an additional indication for drainage.

Such methods of treatment, however, are to be regarded as accessory and to be employed only in the light of the information given by diagnostic lumbar puncture. The guiding principle in routine treatment will be to provide optimum conditions for the natural recovery of damaged cerebral tissues—that is, absolute rest from stimulation (aided by sedatives) in the early stages, and a carefully graduated and prolonged convalescence.

PROGNOSIS.

The ultimate prognosis in these cases is a matter of extreme difficulty. The gross disturbance of cerebral function seen in the early stages must be due to recoverable damage. But there is abundant clinical and some pathological evidence to show that there is nearly always some residual injury of a permanent kind. My own observations have taught me that among manual workers, if clouding of consciousness has persisted for longer than 24 hours after the injury, the chances of an ultimate return to full work are not greater than one in three.

Post-traumatic Cerebral Syndrome.

I would direct attention next to that group of symptoms which may be observed either in the convalescent stage after a severe injury with traumatic stupor or after a minor injury with or without concussion, and which, following Foerster, we may call the post-traumatic general cerebral syndrome. Here again we are confronted with a clinical picture in which the signs of focal cerebral damage are as a rule lacking.

The organic basis of this condition, long emphasised by Duret, has more recently been shown to comprise minor degrees of damage to the nerve-cells and fibres of the same kind as that already described in traumatic stupor (Rosenhagen), and changes in the pressure and circulation of the cerebro-spinal fluid (Bielschowsky). I have not time to refer to this important work in detail, but propose to select one or two clinical problems from this field for consideration.

The first is the extreme frequency of the symptom of vertigo. This symptom, particularly experienced

on stooping or on quick turning of the head, is as a rule unassociated with any deafness or tinnitus. Are we then dealing with a labyrinthine lesion or with damage to the structures of the brain-stem? If the latter, what is the explanation of the frequency of this system? It may possibly be found in the hypothesis of Duret.

INDIRECT INJURY TO BRAIN-STEM.

As the result of experimental work in animals and pathological observation in man, he concluded that in all cases of blunt head injury an important rôle was played by the cerebro-spinal fluid in the transmission of the force of the blow to the intracranial tissues as a whole. He observed that the structures in relation to the walls of the ventricles, and especially the aqueduct of Sylvius and fourth ventricle, suffered severely, and supposed this to be due to momentary distension of these cavities by displacement of cerebro-spinal fluid. If then we regard the vertigo as evidence of injury to the brain-stem, we may find in Duret's hypothesis an explanation of the frequency of this symptom after major or minor head injury. There is another symptom of not infrequent occurrence which may have a similar explanation: diplopia of a nuclear type. I have notes of ten cases of minor head injury (without fracture) in which diplopia was complained of during the first two or three days. Unfortunately, a detailed ophthalmological observation at the time was only possible in three. In two of these the ophthalmologist reported paresis of one superior rectus, and in the other there appeared to be paresis of one inferior rectus. In two of the others the complaint has been of diplopia on looking upwards only.

Occasionally the clinical picture of brain-stem disturbance may be much more definite. For example:—

A male, aged 19, was struck on the left parietal region on May 1st, 1930, by a cricket-ball coming from above and behind. There was no scalp wound. He was knocked down, dazed, but not unconscious. He attempted to rise but could not do so, and lay on the ground for seven or eight minutes. He then got up, changed from flannels into ordinary clothes, and went home by tram, a journey of 40 minutes. During this time he felt sick, but had no other symptoms. Arriving home he went to bed and then vomited. Subsequently he continued to vomit after every meal. He also experienced headache of two kinds: the first a continuous pressure at the back of the head, faint and intermittent; the second, attacks of pain which he referred to the forehead and described as being a pressure like that of a 20 lb. weight inside and acting downwards, lasting five minutes at a time. This latter was brought on by stooping or walking about. Shifting from the horizontal to the sitting position quickly brought it on, but change in the reverse direction gave relief.

On May 3rd, 1930, as his symptoms continued, he got up to come to hospital. He then felt as if his head were going round, and found his gait reeling and unsteady. On examination he showed a slight nystagmus, more to the right than to the left. His gait, with eyes open, appeared normal. Standing with eyes shut, his head tended to fall with the occiput to the right shoulder, and he swayed to the right and back. All deep reflexes were present and equal; the abdominals were diminished on the left, the plantar responses flexor. He was admitted to hospital and put to bed.

On May 8th, 1930, nystagmus, especially to the right, was marked; abdominal reflexes were absent. He had had no vomiting or headaches since admission to hospital. On May 12th, 1930, he had been allowed to sit up in a chair on the previous day. After an hour or so violent headache and dizziness supervened. On examination, in addition to the nystagmus, he showed absence of all tendon-jerks in the upper limbs; knee- and ankle-jerks were obtained with difficulty; abdominals were present on the right, absent on the left; the right plantar response was absent, left flexor. Lumbar puncture showed a clear fluid; pressure 240 mm. of water; no cells; protein, 0·07 per cent.

On May 22nd, 1930, nystagmus was coarse and slow to the right; fine and rapid to the left; tendon-jerks in upper limbs present and equal; right upper and lower abdominals absent; left upper and lower abdominals showed an occasional twitch; knee-jerks present, but sluggish; plantar responses flexor; no headache or vomiting. He subsequently developed measles, and was transferred to another hospital; there he had pneumonia, and therefore was not out of bed until July 9th. He declared himself free from symptoms at the time of examination (July 16th, 1930). He showed slight nystagmus to the right only, and no abnormality of posture or gait. All tendon-jerks were present and equal; abdominal reflexes present and equal, and plantar responses flexor. One year later he reported himself as back at full work (manual) and well, except for occasional headaches.

Types of Headache.

Among the several varieties of headaches encountered in this general post-traumatic state I shall attempt to distinguish three groups.

The first is that complained of by the patient in terms of discomfort rather than pain—a continuous sense of numbness or pressure, aggravated by all kinds of mental stimulus, whether internal—e.g., worry over incapacity—or external (noise, bright light). This is the kind of headache met with in psychogenic states, but also in certain psychoses—for instance, the toxic group and the depressive—and may be considered as one of the reflections in consciousness of general cerebral incapacity.

A second variety, often associated with the first, is equally frequent and of a quite different character. It is complained of as throbbing, piercing, or aching, is localised rather than diffuse, occurs in bouts, usually of brief duration, and is aggravated by change of posture and physical effort as well as by mental stimuli. This kind of headache is often referred to the situation of the initial injury and is sometimes associated with superficial tenderness. Its character and relation to postural change and effort indicate dependence upon some local physical cause, and the recent observations of Penfield, Bielschowsky, and others suggest that this may be found in the shape of loculation in the subarachnoid mesh or ventricular system.

A third and relatively uncommon variety of post-traumatic headache is that which appears in bouts of considerable duration and severity, and has the bursting quality and association with vomiting which suggests a hydrocephalic state. A bout of this kind may be provoked by alcoholic excess or by a severe physical effort—e.g., cranking a refractory automobile. The liability may remain for a short time only after the injury or may persist indefinitely. Assuming the basis of this kind of headache to be a hydrocephalus, is this obstructive—a secondary effect of brain-stem contusion—or is it communicating—due to an increased secretion or defective absorption of cerebro-spinal fluid? Certain observers have postulated a traumatic hydrocephalus of the communicating variety. The following case, recorded by my clinical assistant at Guy's Hospital at the time (Dr. N. L. Lloyd) is the most suggestive I have met with in this connexion.

A male, aged 4, was admitted to hospital unconscious after a severe head injury. He showed bruising behind and below the left mastoid and over the left frontal region. There was no clinical or X ray evidence of fractured skull. There was no striking abnormality of the cranial nerves. The muscles were flaccid with absent deep reflexes and bilateral extensor plantar responses. The cerebro-spinal fluid was intimately mixed with blood and showed a pressure of 300 mm. of water. He remained unconscious for two days and drowsy for a further four days. Subsequently he made a rapid recovery, and was discharged from hospital apparently well a month after his accident.

Five weeks after the accident the cerebro-spinal fluid pressure was 225 mm. of water; no excess of cells or protein.

Eight weeks after the accident the pressure was 230 mm.; constituents normal. Following this he had a severe bout of headache, with drowsiness and vomiting, for which he was admitted to hospital, when a definite swelling of both optic discs was noted. The symptoms disappeared after a day or two, and he returned to a state in which he appeared normal in every way. Further examination 13 weeks after the injury showed a pressure of 300 mm., notwithstanding the absence of all symptoms. Papilloedema was still visible. Subsequently the boy attended school and has remained well during the succeeding five years.

Thus it appears after a head injury, in the absence of any fracture of the skull or demonstrable focal lesion, a state of increased intracranial pressure may persist for at least three months. Equally striking in this case is the comparative absence of symptoms.

If the lines of clinical distinction between these varieties of headache be valid they will serve as guides to differential treatment. The "psychogenic" type of headache will be amenable only to general measures of cerebral rest, including the removal, when present, of litigation worries. The intermittent, localised variety of headache, related to change of posture, may, in the light of Penfield's and Bielschowsky's work, prove capable of relief by air injection or in severe cases by operation. The rarer hydrocephalic form invites treatment by repeated lumbar puncture.

Delayed Symptoms.

There is one other aspect of the clinical problem which compels attention. In not a few cases the symptoms—sometimes severe—of cerebral injury may supervene after a considerable latent interval. The subsequent clinical course suffices to exclude late meningeal hæmorrhage (subdural hæmatoma) as the cause. For example:—

A male, aged 29, on May 7th, 1930, was struck on the head by the blunt end of an axe weighing 7 lb. He did not lose consciousness. The lacerated scalp was sewn up at hospital. After resting for 36 hours he returned to work as a labourer for five days without symptoms. On the eighth day after the accident he complained of severe headache, continuous, dull, bursting, frontal, aggravated by swinging a hammer or lying down; better when standing up; also of an intermittent stinging pain in the right sub-occipital region, unrelated to circumstance, occurring every two or three hours and associated with intense giddiness of a dizzy, drunken nature.

When seen on the tenth day after the accident he showed the following signs: right pupil larger than left; nystagmus, more to right than left; generalised hypotonia; tendon-jerks in upper limbs absent; in lower limbs sluggish; superficial reflexes normal.

He was admitted to hospital and treated with rest and hypertonic salines. On the fifteenth day he showed nystagmus, coarse and slow to the right, rapid and finer to the left. All deep reflexes were absent, even with reinforcement. The abdominal reflexes were feebly present on the right, absent on the left; both plantar responses were absent. The cerebro-spinal fluid was clear, pressure 180 mm. of water, and contained no trace of blood; protein, 0·05 per cent. This patient made a slow recovery with rest and graduated convalescence, and returned to light work four and a half months after the accident.

The occurrence of such cases is undisputed. What is the pathology of the latent interval? Marchand has suggested that it is a gradually developing reaction of the cerebral tissues to areas of necrosis produced by the initial injury—a process which he has named traumatic encephalitis. A similar view has been put forward by Osnato and Giliberti. The experimental observations of Rio-del-Hortega and Penfield go some way towards supporting this hypothesis. Nevertheless the intensity of the symptoms in such a case as I have related, and the acuteness of their onset, suggest that other factors also—probably hydrostatic—are active.

It is evident that, despite the important work which has already been done, the study of brain injuries offers a rich field of inquiry both to the clinical neurologist and to the neuropathologist.

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VACCINIA AND THE PASCHEN BODY:

INFECTION EXPERIMENTS WITH CENTRIFUGALISED VIRUS FILTRATES.

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IMPROVEMENTS in technical methods of virus research have led to renewed study in recent years of the claim put forward by Paschen so long ago as 1906 that the elementary bodies discovered by him in material from vaccinial lesions might prove to be the actual ætiological agents. The present position may be thus summarised:—

(1) The elementary bodies which are readily demonstrated by appropriate staining methods are invariably found in enormous numbers not only in the characteristic skin exanthem, but also in those gross organ lesions which may follow the inoculation of highly potent virus in experimental animals.

(2) Bechhold and Schlesinger (1931) in an attempt to estimate the size of the infective virus particle in vaccinia by physical calculations based on high speed centrifugalisation experiments with virus suspensions, obtained a figure (0·21μ–0·23μ) for the diameter of the virus particle which agrees closely with the many recorded measurements of the stained Paschen body—viz., 0·2μ–0·25μ. The actual diameter of the naked Paschen body is doubtless less than 0·2μ and one of us (L.) has observed that the stained bodies contained in pure suspension in formalised saline are distinctly smaller than in their native element where their natural size is enhanced by deposition of stain and by the presence of serum proteins in the menstruum. Moreover, from the recently published experiments of Elford and Andrewes (1932) on the filtration of vaccinia virus through collodion membranes of varying porosity, the calculation is made that the size of the infective virus particle is of the order of 0·125μ–0·175μ and thus considerably less than that derived from Bechhold's centrifuge experiment.

Even direct measurements of naked bacteria and cocci are notoriously subject to error and such error must be still greater with such small objects as Paschen bodies. It would seem hardly likely, however, in view of the estimated range of diameter based on filtration and centrifuge experiments, that any claimant other than the well-known Paschen

body is likely to be forthcoming for the position of infective virus particle.

(3) One of us (Ledingham, 1931, 1932) has reported that pure suspensions of elementary bodies in vaccinia and fowl-pox can be obtained in an indifferent medium of formolised saline and that such suspensions are specifically agglutinated by the serum of vaccinated animals. Their agglutination can be readily followed in hanging drop preparations with a two-thirds inch objective and the stained clumps are found to consist wholly of elementary bodies. Moreover, after a single dose of virus, agglutinins appear in the serum, rise to a maximum, and slowly fall precisely as do agglutinins in response to any bacterial antigen.

(4) The elementary bodies have recently been shown by Nauck and Paschen (1932) to increase in numbers in cultures of vaccinia virus grown in vitro in the presence of testicular tissue, and we may state here that we have been able to demonstrate the presence of numerous Paschen bodies in stained preparations of vaccinia cultures grown by Eagles and McClean (1931) in a cell-free medium.

OBJECT OF PRESENT EXPERIMENTS.

The experiments here recorded were undertaken to secure further evidence in support of the claim for the Paschen body to be the actual infective agent. They are substantially amplifications of such experiments as those of Ward (1929) and Tang (1930) who followed up their successful filtrations of vaccinia virus through low-grade candle filters by centrifuging the filtrates and demonstrating a concentration of virus in the bottom layers. The results certainly supported their view that the infective particle may be "of considerable size" and that the nature of the material submitted to centrifugalisation rather precluded the possibility of virus being simply adsorbed on inert particles which had escaped the filter. Centrifugalisation of carefully prepared suspensions of neuro-vaccine by Bland (1929) also supported strongly the view that the virus of vaccinia can be thrown down by the centrifuge given sufficient time and speed.

EXPERIMENTAL METHODS.

Our experiments have all been carried out with Berkefeld "V" filtrates of vaccinia virus which have been submitted to centrifugalisation with a new model high speed centrifuge (manufactured by Baskerville and Lindsay, Manchester) capable of speeds up to 14,000 revolutions per minute with a 10 c.cm. load. One of us (E.) was responsible for the centrifugalisation and the experimental testing of the various supernatants and deposits, while the other undertook the examination of the stained deposits for the presence of Paschen bodies.

For the cutaneous inunction of rabbits two strains of virus were used—viz., a testicular strain of rabbit origin and a purely dermal strain of sheep origin. Some few experiments were also carried out with testicular tissue infected with neuro-vaccine, but these on the whole were less satisfactory, so far as completeness of deposition of virus was concerned, possibly because the filtrates were heavily charged with hæmoglobin and perhaps also because the Paschen body content of the filtrates was very high. The filtration technique was that employed in former experiments by Green and Eagles (1931).

The lapine was removed from the backs of rabbits on the third or fourth day after inunction. The pulp was thoroughly ground in a mortar, no sand or other material being used to facilitate grinding. After suitable dilution with distilled water the virus suspension was lightly centrifugalised, then passed through coarse filter paper, and finally through a Berkefeld "V" candle. All filtrates used were water-clear, bacteriologically sterile, and of fair potency when tested by intradermal inoculation in the rabbit.

EXPERIMENTAL DATA.

The three experiments (A, B, and C) recorded in detail below are selected from a set of about 15 in all, because they illustrate best the effect of variation in speed and time of action of centrifuge on the deposition of virus from filtrates and on the further purification of macroscopically visible or invisible deposits by repeated saline washings.

Experiment A (Table I.).—To determine how far concentration of virus contained in filtrate was affected by centrifugalisation of 4 c.cm. filtrate for 30 min. at 10,000 rev. per min.

After removal from the centrifuge the supernatant fluid was carefully pipetted off in 1 c.cm. amounts. The bottom c.cm. was found to be in contact with a faintly visible deposit which was incorporated with it by thorough mixing after being scraped from the glass with a platinum spatula. Samples from the upper c.cm., the third c.cm., and the fourth c.cm. containing the scraped off deposit were titrated for potency on the rabbit by intradermal inoculation in parallel with the unspun filtrate as control. Table I. shows that the fourth c.cm. and the third c.cm. contained by far the major portion of the virus, the end-point being not nearly reached in the case of the former. The figures in the Table represent the diameters (or average diameters) of each reaction at its height, but it should be borne in mind that for comparative purposes the cubes of the diameters are more strictly appropriate.

Examination for Paschen bodies.—Film from fourth c.cm. showed very large numbers of elementary bodies mostly in carpets but occasionally in agglomerations. In the upper and third c.cms. only very few bodies could be detected.

TABLE I.—*Experiment A.*

Material used: Filtrate of lapine obtained by skin inunction of rabbit with neuro-testicular virus.

Potency Tests of Supernatants and Deposits.

Dilution.	Control. Unspun filtrate. Day—4th	Control. Unspun filtrate. 5th	4th c.cm. containing incorporated deposit. 4th	4th c.cm. containing incorporated deposit. 5th	Upper c.cm 4th	Upper c.cm 5th	3rd c.cm. 4th	3rd c.cm. 5th
10^{-1}	25 m.	30 m.	35 m.	40 m.	20 m.	22 m.	20 m.	25 m.
10^{-2}	20 m.	25 m.	30 m.	35 m.	15 m.	15 m.	18 m.	20 m.
10^{-3}	15 m.	15 m.	25 m.	32 m.	10 m.	10 m.	13 m.	13 m.
10^{-4}	10 m.	10 m.	15 m.	15 m.	±	±	5 m.	8 m.
10^{-5}	±	5 m.	18 m.	18 m.	n	n	±	5 m.
10^{-6}	n	n	12 m.	12 m.	n	n	n	n

m. = millimetre. ± = reaction appearing faintly red but not measurable.

Experiment B (Table II.).—Centrifugalisation for one hour periods at 12,000–14,000 rev. per min.

The entire supernatant was removed, care being taken to avoid disturbance of deposit in contact with the glass. This supernatant was again spun at the same speed for one hour. It was removed from possibly present but invisible deposit and spun a third time for one hour. In this way three deposits were obtained for titration purposes along with samples of the various supernatants and the unspun filtrate. Only the first deposit was visible to the naked eye. The three deposits were carefully scraped and mixed each with three drops of saline from a standard drop pipette. Table II. shows that the major portion of the virus was present in the first deposit after one hour's spinning, while the second and third deposits contained diminishing amounts of virus. The supernatant which had been submitted to two hours' spinning contained only a trace of virus, but after three hours' spinning was entirely devoid of activity.

Examination for Paschen bodies.—Film from first deposit showed colossal numbers of elementary bodies mostly entirely in big and little aggregations and attached to or in the neighbourhood of amorphous flaky matter. The high speed of spinning had obviously caused packing of the bodies

on the glass. The second deposit contained only occasional small packets, while the third appeared entirely free of bodies. In the two supernatants elementary bodies could not with certainty be detected.

TABLE II.—*Experiment B.*

Material used: Filtrate of lapine obtained by skin inunction of rabbit with neuro-testicular virus.

Potency Tests of Supernatants and Deposits.

Dilution.	Control. Unspun filtrate.		1st dep.		2nd sup.		2nd dep.		3rd sup.		3rd dep.	
	Day—4th	5th	4th	5th	4th	5th	4th	5th	4th	5th	4th	5th
10^{-1}	25 m	25 m	45 m	50 m	±	5 m	15 m	20 m	n	n	5 m	8 m
10^{-2}	20 m	25 m	40 m	45 m	n	n	10 m	15 m	n	n	n	±
10^{-3}	15 m	20 m	30 m	35 m	n	n	±	8 m	n	n	n	n
10^{-4}	12 m	15 m	25 m	30 m	n	n	±	±	n	n	n	n
10^{-5}	8 m	10 m	20 m	25 m	n	n	n	n	n	n	n	n
10^{-6}	±	5 m	15 m	20 m	n	n	n	n	n	n	n	n

dep. = deposit; sup. = supernatant.

Experiment C (Table III.).—To determine the potency of repeatedly washed deposit. Centrifugalisation for one hour at 12,000–14,000 rev. per min.

A small amount of fluid inevitably remains in contact with the deposit when the supernatant is removed. In order to free the elementary bodies from this fluid the supernatant was entirely removed and the deposit carefully incorporated with 4 c.cm. of salt solution. This saline suspension was now spun for one hour and the deposit again washed in saline and re-spun. This twice-washed deposit was incorporated in three drops of saline and along with the second saline supernatant and the primary supernatant removed from the first deposit, submitted to potency test. Table III. shows that the virus was concentrated in the twice-washed deposit, while the second saline washing was entirely free of virus. A small amount of virus was, as might be expected, present in the primary supernatant.

Examination for Paschen bodies.—Films of the final twice-washed deposit showed colossal numbers of elementary bodies mostly in small and large packets, but occasionally in large sheets. In the other fluids they were not definitely detected.

TABLE III.—*Experiment C.*

Material used: Filtrate of lapine obtained by skin inunction of rabbit with lymph of ovine origin.

Potency Tests of Supernatants and Deposits.

Dilution.	Control. Unspun filt.		Twice-washed dep.		Saline sup.		Primary sup.	
	Day—4th	5th	4th	5th	4th	5th	4th	5th
10^{-1}	20 m.	20 m.	22 m.	25 m.	n	n	6 m.	8 m.
10^{-2}	13 m.	13 m.	20 m.	20 m.	n	n	5 m.	5 m.
10^{-3}	11 m.	11 m.	15 m.	15 m.	n	n	5 m.	5 m.
10^{-4}	n	n	15 m.	15 m.	n	n	n	n
10^{-5}	n	n	12 m.	12 m.	n	n	n	n
10^{-6}	n	n	±	5 m.	n	n	n	n

If the Paschen bodies are responsible for the potency of deposits it might be expected that the great concentration of virus in the latter, as shown by titration, would be reflected in the number of bodies found therein, and further, that deposits and supernatants which vary in potency would be associated with similar variations in their Paschen body content. The usual technique was to dip a 2 mm. platinum loop into the fluid to be tested for potency (whether supernatant, or bottom fluid with incorporated deposit, or washed deposit made up with saline). After withdrawal the fluid was spread as thinly as possible on a slide and treated and stained by the approved technique (see Med. Res. Council's System of Bacteriology, 1931, vol. ix., p. 132). Invariably the film from the first deposit has shown the presence of what would appear to be the great bulk of the Paschen bodies originally contained in the fluid spun, while in other fluids (primary supernatants and washings) only small numbers of bodies can be detected with certainty. It has been the practice of those experienced in the staining of elementary bodies never to diagnose their presence unless they occur in clearly recognisable collections large or small. Some method of enumeration is desirable, and doubtless if it were possible to disperse the collections and to obtain a homogeneous distribution the problem of enumeration would be greatly simplified.

DISCUSSION.

The representative experiments we have here recorded on the effect of high-speed centrifugalisation on virus filtrates and on the broad correlation of potency of fluids tested with their Paschen body content leave, in our opinion, no escape from the conclusion that these deposits, visible or invisible, owe their potency to the presence of Paschen bodies in them. The speed and the period of centrifugalisation are important for securing a virus-free supernatant. A speed of 10,000–11,000 rev. per min. acting for one hour has been found to result either in a concentration of the virus in the lower layer of the fluid or in a deposit which is so lightly attached to the glass that the supernatant fluid cannot be completely removed without disturbing the deposit. If a small quantity of gelatin is placed in the tip of pointed tubes before the virus filtrate is added, the elementary bodies can be held. The presence of gelatin however does not favour the search for the bodies in stained films. The experiments in which deposits were submitted to repeated washings in saline are, in our view, particularly convincing, inasmuch as the stained preparations of the potent fluids showed rich carpets of elementary bodies and an almost complete absence of other stainable matter formed or amorphous. As the saline menstruum itself was proved to contain no virus the conclusion is irresistible that the infecting agent is the Paschen body, though it is always possible to assume that the true virus may be something attached to the surfaces of Paschen bodies, but incapable of existing apart from them or of being dissociated by mechanical means such as repeated washing. In the present state of knowledge such criticism can have little cogency and, indeed, might be logically applied to any generally accepted causal bacterium on the ground that it is merely the vehicle of some lesser hypothetical agent.

With the further knowledge from the serological side (Ledingham) and the demonstration by Nauck and Paschen that in successful artificial cultures Paschen bodies are present in large numbers—a claim which we have been able to confirm for the cultures obtained by Eagles and McClean in cell-free media—the evidence in support of the Paschen body as the ætiological agent of vaccinia would seem to be reasonably complete. It is of very great interest in this connexion that Bedson (1932) has been able, by very similar means to those employed in this work, to secure evidence that the minute bodies found in psittacosis represent in all probability the actual infective agents. To conclude, it remains to be shown that artificial cultures starting from pure seedings of Paschen bodies are possible, and doubtless

knowledge of the manner of growth and division of the elementary body will then be forthcoming.

SUMMARY.

(1) By high-speed centrifugalisation it has been possible to deplete Berkefeld filtrates of vaccinia virus almost entirely of their virus content and to recover the great bulk of the virus in deposits consisting in the main of Paschen bodies.

(2) Such deposits after repeated washings in saline retain their potency, while the saline menstruum in which the bodies are suspended has been entirely depleted of virus.

(3) In the light of these experiments the present status of the Paschen body is discussed, and the conclusion is reached from all the evidence now available that the cause of vaccinia is the Paschen body.

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A REPORT ON FIFTY CASES OF MALARIA TREATED WITH ATEBRIN.

A NEW SYNTHETIC DRUG.

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ATEBRIN, originally called erion, has been produced recently by the makers of plasmoquine. Its composition has not been divulged, and the properties of the drug are being investigated in Europe, Asia, and America. According to Schulemann,[1] atebrin is related chemically to plasmoquine, and both drugs have been evolved by using the structural formula of methylene-blue as a starting-point.

Dr. O. Urchs, of Calcutta, has kindly supplied details of preliminary tests made with atebrin in Europe, and has requested the Institute of Medical Research, Kuala Lumpur, to undertake an investigation concerning the efficacy of this new drug in the treatment of malaria. Atebrin was received in the form of tablets, each of which was said to contain 0·1 g. of the drug. The dosage recommended was about one-sixth that of quinine. The drug is somewhat bitter to taste and is readily soluble in water, producing in it a bright yellow colour. Unlike plasmoquine, and like quinine, atebrin shows fluorescence in high dilution under ultra-violet radiation.

An inquiry regarding the properties of this drug is still proceeding. So far, 50 cases of malaria have completed seven days' treatment with atebrin. Subsequently, the patients have been kept under daily observation as long as possible. The 50 cases mentioned comprised 16 benign tertian, 24 subtertian, and 10 quartan, and consisted of male Tamils, Chinese, and Sikhs whose ages ranged from 6 to 50 years. The majority gave a history of repeated attacks of malaria occurring over a period of six months or more; 46 similar individuals, suffering from malaria, were treated for seven days with quinine bihydrochloride, grs. 30 daily, in the form of a mixture. These control cases were used for comparison in all particulars. Fuller details, such as the degree of infection, method of treatment, &c., regarding both series of cases, are given later.

COMPARISON OF PARASITOCIDAL PROPERTIES.

Thick blood films from each case were examined daily. In both the atebrin and quinine-treated cases the asexual parasites disappeared from the blood, as a rule, within the seven-day treatment period, but quartan gametocytes tended to persist after the seventh day, later to disappear; while in the subtertian cases the gametocytes seemed unaffected by the drugs. For this reason the findings regarding quartan and subtertian gametocytes are omitted from Table I., which compares the average period of persistence of all parasites in the benign tertian cases and of the asexual parasites only in the subtertian and quartan series.

TABLE I.—*Parasitocidal Properties Compared.*

		Quinine bihydrochloride grs. 30 daily (2·0 g.) for 7 days.		Atebrin grs. 3 to 6 daily (0·2 to 0·4 g.) for 7 days.	
		Cases.	Days.	Cases.	Days.
Blood parasites.*	B.T.	17	3·6	16	2·4
	S.T.†	9	2·8	24	3·5
	Q.†	20	5·8	10	4·4

* Average number of days parasites persisted in the blood (thick films), including day when treatment commenced.
† Denotes trophozoites and schizonts only.

With regard to the rate of destruction of malarial parasites in the blood, atebrin appears to compare very favourably with quinine in the treatment of benign tertian and quartan malaria. The trophozoites of *P. falciparum*, however, persisted longer among the atebrin-treated cases.

COMPARISON OF THE DURATION OF THE FEBRILE PERIOD.

The temperature of each patient was taken every four hours, and the hour when treatment commenced was noted on the temperature chart. The duration of the febrile period was estimated from the time when the first dose of the drug was given, to the time when the temperature ceased to rise to 99° F. or over. In some cases,* despite the presence of large numbers of parasites in the blood, the temperature remained below 99° F., and these cases are omitted from Table II.

TABLE II.—*Duration of the Febrile Period.*

		Quinine bihydrochloride. (Same dosage as Table I.)		Atebrin.	
		Cases.	Hours.	Cases.	Hours.
Fever*	B.T.	12	30	14	33
	S.T.	8	30	20	34
	Q.	12	58	10	43

* Average period of persistence of fever (temp. 99° F. or over) from commencement of treatment.

RELAPSE AFTER TREATMENT.

The term relapse is used, in this instance, to denote the reappearance of parasites in the blood, with or

* Patients who are infected with malarial parasites but who remain afebrile for long periods without treatment are not infrequently encountered in Malaya. Some of them exhibit an extraordinary degree of tolerance to the presence of comparatively large numbers of malarial parasites in the blood.

without symptoms. After treatment ceased, thick blood films were taken daily from all patients who could be induced to remain in hospital under observation. In one case benign tertian parasites reappeared in the blood nine days after completion of a seven-day course of quinine treatment (grs. 30 daily). Accordingly, in Table III., only those cases who remained under subsequent observation for nine days or more have been included.

TABLE III.—*Relapse After Treatment.*

—	Quinine-treated cases.			Atebrin-treated cases.		
	B.T.	S.T.	Q.	B.T.	S.T.	Q.
Cases observed 9 days or more after treatment ceased	11	6	17	4	9	6
Period of observation in days. Limits	9–28	9–21	9–48	10–47	9–43	9–66
Period of observation in days. Aver.	14	16	22	24	17	25
Proportion of relapses ..	6/11	2/6	5/17	0/4	0/9	0/6
Percentage of relapses ..	55	33	29	0	0	0
Day when relapse occurred. Limits	9th–18th	13th–15th	15th–27th	No relapses.		
Day when relapse occurred. Aver.	14th	14th	20th			
Form of parasite found in blood on relapse ..	6/6*	2/2*	3/5* 2/5†	,,		

* Relapsed with B.T. parasites. † Relapsed with quartan parasites.

Thirteen relapses were noted among 34 quinine-treated cases.† Among a total of 19 cases treated with atebrin and observed, on an average, over somewhat longer periods, no relapses occurred; and, although the numbers observed were comparatively small, the results appear to indicate that atebrin may be superior to quinine in preventing relapses.

ACTION OF QUININE AND OF ATEBRIN ON GAMETOCYTES.

Disappearance of the gametocytes during treatment.—In the benign tertian cases, treatment with atebrin brought about a rapid disappearance of gametocytes, and, in this respect, it was similar to quinine. The effect of both quinine and atebrin on quartan gametocytes was less marked than on those of *P. vivax*, but in no case were the gametocytes of *P. malariæ* found in the blood later than the twelfth day after the inception of treatment, although administration of the drugs had ceased on the seventh day. The resistance of the gametocytes of *P. falciparum* to quinine is well known, and they may persist for some weeks after the trophozoites have disappeared, even though the quinine treatment is continued. In the two series of cases under discussion, neither quinine nor atebrin appeared to have any directly destructive effect on the gametocytes in the blood of the subtertian patients.

Interference with the viability of gametocytes.—Plasmoquine has been shown to affect the viability of subtertian gametocytes in such a way as to prevent them developing further in the mosquito. With this in mind, experiments were undertaken to find whether atebrin affected the viability of gametocytes in the same way. Again, cases treated with quinine were used as controls, and batches of anopheline mosquitoes were fed at certain times during the period of treatment on (*a*) cases treated with quinine, and (*b*) cases treated with atebrin. Neither drug was found to affect the viability of subtertian or benign tertian gametocytes, and the results are given in Table IV.

TABLE IV.—*Showing Lack of Effect of Quinine and Atebrin on the Viability of Gametocytes.*

(*a*) *Quinine** (grs. 30 daily).

Gametocyte carriers of—	Gametocytes in blood (per c.mm.).	Days of treatment given.	Total of drug given.	Mosquitoes infected (oöcysts and sporozoites).
P. vivax ..	58	1·3	grs. 40	*A. maculatus*
P. falciparum	277	13	grs. 390	,,
(*b*) *Atebrin** (0·2 to 0·4 g. daily).				
P. vivax ..	1300	1·3	0·3 g. (grs. 4½)	*A. hyrcanus* var. *sinensis* *A. subpictus* var. *malayensis*
P. falciparum	6440	7	2·8 g. (grs. 43)	*A. vagus* *A. kochi* *A. aconitus* *A. philippinensis*
P. falciparum	640	7	2·1 g. (grs. 32)	*A. kochi*

* In each case one dose of drug was given 30 minutes prior to feeding mosquitoes.

TOXIC SYMPTOMS.

Of the 50 patients treated with atebrin, two complained of headache and four of abdominal pain. Headache in the supra-orbital region occurred on the sixth day of treatment in one case, and two days after a seven-day course of treatment had been completed in the other.

Abdominal pain was severe in three cases and mild in the remaining one. It was intermittent in character and lasted for some hours. The pain was unaccompanied by vomiting, and occurred in the epigastric region as early as the fourth day of treatment, and as late as the fifth day after treatment had been stopped. It was difficult to be sure, in all cases, that the headache and abdominal pains were due to atebrin, but there was reasonable certainty that the severe epigastric symptoms were caused by the drug.

In seven cases a yellow discoloration of the skin, whites of the eys, or both, was noted. This seemed to be due to a dyeing effect of the drug on the tissues and not to jaundice, for serum from such cases, when tested, did not show excess of serum bilirubin. The depth of colour of the skin varied from a faint yellow, occurring in six cases, to a more marked yellow in one case. This discoloration of the skin or sclerœ made its appearance on the sixth to the ninth day (average eighth day—i.e., the day after treatment ceased), and remained for periods varying from 8 to 15 days, when the tissues regained their normal colour. All seven cases had received comparatively

† Among the cases treated with quinine, the form of parasite occurring on relapse seems to deserve comment, for in all cases except two benign tertian parasites were found. Previously, Fletcher [1] in Malaya noted the frequency with which benign tertian parasites were present in the blood during a relapse, although when the patients first came for treatment other forms of parasite were found. Similar observations have been made in other countries; and the possibility that one species of malarial parasite becomes converted into another has been seriously considered as an explanation of these findings. As a more likely explanation, some authorities put forward the hypothesis that, in certain mixed infections, one species becomes predominant during the acute phase of the malarial attack and remains predominant for some time. If this may be accepted, the results given in the table above suggest that an unexpectedly large proportion of malarial infections in Malaya are mixed; but, during the acute phase, when the patient seeks treatment, one or other of the parasite species predominates and is the only one found; the other, or latent form of parasite, is probably sporulating quietly in a backwater of the blood stream, or occurs in such small numbers as not to be evident in thin or thick blood films. These latent forms may possess a greater resistance to the action of drugs or, by reason of their position in the body, may fail to be subjected to the drug in its usual concentration; either possibility would explain their tendency to appear on relapse.

large doses of the drug (0·4 g. daily), and in all the excretion of the drug was found to be delayed; that is, it first appeared in the urine from the sixth to the thirteenth day (average eighth day), whereas, in cases showing no tinting of the skin or scleræ, the urine generally showed the characteristic colour of atebrin about the third or fourth day.

Atebrin did not appear to give rise to albuminuria, and in two cases of quartan malaria an initial albuminuria disappeared during administration of the drug.

GENERAL.

Notes on patients investigated and methods used.—Further details regarding the patients under treatment are given in Table V.

TABLE V.

		Quinine-treated cases.	Atebrin-treated cases.
Age	Range	18 to 45 years	6 to 52 years
	Average	29 „	29 „
Body-weight	Range	88 to 133 lb.	39 to 144 lb.
	Average	108 „	105 „

M.I.*	Cases.	T.	S.	G.	Cases.	T.	S.	G.
B.T.	17	5,841	1,000	333	16	5,426	107	184
S.T.	9	54,371	0	60	24	23,709	50	84
Q.	20	2,579	1,136	128	10	3,028	480	89

* M.I. = Average degree of malarial infection on first day of treatment, expressed as numbers of trophozoites, schizonts, and gametocytes per c.mm. of blood.

The patients were isolated in a special ward and were examined twice daily during the period of treatment and observation. Treatment was preceded by routine purgation. The drugs were given twice daily and, when the patients received 0·3 g. of atebrin each day, 0·2 g. was given in the morning and 0·1 g. in the evening. Every precaution was taken to see that the drugs were actually swallowed and were not vomited subsequently. The temperature was taken every four hours, and the following observations were made daily: Spleen measurements, hæmoglobin percentages (Dare), and counts of the numbers of parasites in thick blood films, using the fowl-corpuscle method (Sinton [3]). Each patient was weighed daily, and the urine was examined each day for the presence of albumin, quinine, and atebrin.

Urine tests.—In the information accompanying the supply of atebrin it was stated that "by means of ether atebrin can be extracted from urine which has been rendered alkaline, and if the residue resulting from the evaporation of ether is dissolved in concentrated sulphuric acid this assumes a yellow colour, strongly fluorescent." It was found, however, that among patients taking atebrin the characteristic yellow colour of the drug became apparent in the urine by rendering it acid and heating it. This colour was best seen by viewing the urine in the test-tubes from above downwards. Although this was not so delicate a test as the ether extraction mentioned above, daily observations on the urine of atebrin-treated cases showed that the drug appeared in the urine about the third or fourth day after treatment commenced, but could still be detected by this rough test up to the eighth or ninth day after treatment had ceased. These observations seem to indicate that the drug tends to accumulate in the body and to be excreted slowly.

When dissolved in water the yellow colour of atebrin persisted up to dilutions of 1 in 102,000; luminescence under ultra-violet radiation was still apparent in dilutions of 1 in 818,000, while precipitation with Mayer's reagent occurred up to dilutions of 1 in 409,000. The urine of patients taking atebrin did not, however, show precipitation with Mayer's reagent, although showing the yellow colour of atebrin.

It was thought that ultra-violet light might be of use in detecting small quantities of atebrin in urine. This, however, was a failure, for it was found that all specimens of urine, from normal and untreated individuals, contained substances which glowed under ultra-violet light, and these substances interfered with the detection of drugs that were similarly luminescent.

Dosage of atebrin.—Table VI. shows the dosage used among the 50 cases mentioned.

TABLE VI.

Daily dose.	Patients treated. B.T.	S.T.	Q.	Remarks.
				Dose regarded as—
0·2 g.	4	4 + 1 (boy)	2	Too small for adults.
0·3 g.	6	8	5	Adequate for adults.
0·4 g.	6	11	3	Too large for adults.

The inclusion in Tables I. and II. of ten adults treated with 0·2 g. atebrin daily, which is regarded as an inadequate dose, has tended to prolong the average period of persistence of parasites in the blood, also the duration of fever, as shown in these Tables.

The patients receiving atebrin treatment had an average body-weight of 105 lb. (about 48 kg.), which is below the average body-weight of Europeans. It is concluded, from the results observed among the cases treated with daily doses of 0·3 g., that the optimum dose of atebrin for all forms of malaria is probably 0·1 g. per 15 kg. body-weight per day for a period of six to seven days. At the end of this period a good deal of the drug has accumulated in the body and continues to be excreted for a further period of seven days or longer. The malarial parasites are thus probably subjected to the action of the drug for a longer period than the actual period of administration.

General progress of patients.—The two series of cases, treated with atebrin and with quinine, showed similar favourable progress as regards increase in hæmoglobin percentage and body-weight, also in the rate of reduction in the size of the spleen.

SUMMARY AND CONCLUSIONS.

1. Notes are given on 50 cases of malaria treated with atebrin, a new synthetic drug evolved by the makers of plasmoquine. Forty-six cases treated with quinine bihydrochloride were used as controls.

2. Atebrin compares favourably with quinine in ridding the blood of malarial parasites and in relieving symptoms. So far it seems superior to quinine in preventing relapses.

3. Atebrin is not unpleasant to take, but in a small proportion of cases it gives rise to abdominal pains. Where comparatively large doses are used, and excretion of the drug is delayed, a yellowish discoloration of the skin appears, which may remain from 8 to 15 days.

4. Atebrin, like quinine, does not affect the viability of the gametocytes of *P. vivax* or *P. falciparum*. Its use, however, over a period of seven days or less destroys the gametocytes of *P. vivax* with sufficient

rapidity to prevent mosquitoes becoming infected from benign tertian cases within three or four days after treatment commences. Among gametocyte carriers of *P. falciparum* neither atebrin nor quinine may be regarded as an efficient drug in preventing the infection of mosquitoes which have access to such patients under treatment.

5. The optimum dosage of atebrin for all forms of malaria is probably 0·1 g. per 15 kg. body-weight per day, given for a period of six to seven days. Treatment should be preceded by preliminary purgation, and it is suggested that the urine should be examined for the presence of the drug each day in all cases under treatment. Late appearance of the drug in the urine may be taken as an indication that the drug is accumulating in the body in greater concentrations than desirable, and this may give rise to discoloration of the skin or scleræ.

6. If the cost of treatment with atebrin compares favourably with that of quinine, this new drug assumes an added importance, particularly if it is shown definitely to be more effective than quinine in preventing relapses when used for short courses of treatment. Atebrin thus deserves full and widespread investigation, but final opinion regarding its general use in malaria and its toxicity should be withheld pending completion of such investigations.

I am indebted to Dr. A. Neave Kingsbury, Director of the Institute for Medical Research, F.M.S., for permission to undertake the investigation and to publish this paper. Dr. O. Urchs, of Calcutta, has kindly supplied large quantities of atebrin, together with details of preliminary tests made in Europe. I am also indebted to Dr. W. E. Diamond for the privilege of treating with this new drug cases of malaria admitted to the District Hospital, Kuala Lumpur.

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THE TREATMENT BY MARMITE OF MEGALOCYTIC HYPERCHROMIC ANÆMIA

OCCURRING IN IDIOPATHIC STEATORRHŒA (CŒLIAC DISEASE).

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IN an investigation of a group of 15 cases of idiopathic steatorrhœa (cœliac disease) associated with tetany and often with bone deformities [1] two were found to have a hyperchromic megalocytic type of anæmia. In view of the observation of Wills [32] that marmite was as effective as liver extract in the treatment of tropical megalocytic anæmia, it was decided to test its effect in the present cases. The nature and significance of the response obtained by such treatment form the subject of this paper.

INTRODUCTION.

Gee [10] in his original description of cœliac disease states that "cachexia, a fault of sanguification betokened by pallor and a tendency to dropsy, is a constant symptom." Subsequent observers have shown that the blood picture may be extremely variable, depending presumably upon which of the factors essential for hæmopoiesis are lacking. There may be no abnormality.[1 9 16] The majority of cases show a hypochromic anæmia,[9 13 25 28] but 20 cases with a hyperchromic megalocytic anæmia have been reported, and we have a small group with an erythroblastic type of anæmia now under observation.[1]

The recorded cases of megalocytic hyperchromic anæmia in which full blood counts are available are shown in the Table. In addition, Rossier [23] has described three cases in adults of pernicious anæmia associated with diarrhœa, tetany, and disturbances of blood calcium, which were possibly cases of cœliac disease, especially as free hydrochloric acid was present in two. Witts [33] calls his case one of chylous diarrhœa, but since the patient is described as having "such scoliosis that his spine seems to have shrunken," the inclusion in the present group seems justified. The case described by Hampson and Shackle [14] was thought at the time to be one of renal dwarfism, but as her blood-urea was as low as 13 mg. per 100 c.cm. and a trace of albumin in the urine occurred on one occasion only, it is more likely that she was a cœliac dwarf, and she has therefore been included. Thaysen [28] states that 11 of his cases had at one time a hyperchromic anæmia, but no mention is made of the appearance of the red blood-cells. They are not therefore tabulated.

Two cases described by Schaefer [24] and Hegler [15] as non-tropical sprue are also not included, as, though they had severe steatorrhœa and a megalocytic hyperchromic anæmia, it is not clear that they had either tetany or disturbances of calcium metabolism associated with bone deformities.

CASE REPORTS.

CASE 1.—A married woman, aged 40 years (L. H., Reg. No. 40997/1930). All her life she has had attacks of diarrhœa with yellow offensive slimy motions and intervals of relative freedom. She improved when she was 7 years old, but became worse after her only child was born, 11 years ago. The attacks last about five days, when she passes about six stools a day. Between attacks the bowels are open three times daily and she may have to get up four times at night. The diarrhœa tends to become worse in warm surroundings. She first noticed cramps in her hands and feet in June, 1930.

On Feb. 18th, 1928, she was an in-patient under the care of Dr. A. M. H. Gray at University College Hospital for a persistent pustular dermatitis affecting the limbs, face, scalp, and to a less extent the trunk. A pure culture of *Staphylococcus aureus* was obtained from the lesions. She was treated by vaccines, iron, and arsenic, and a variety of liniments and proprietary foods containing vitamins.

On Feb. 22nd, 1930, she became an in-patient under the care of the Medical Unit at University College Hospital, when a diagnosis of pancreatic insufficiency was made. The total fat in the stools at that time was 71·2 per cent., of which 45·2 per cent. was neutral fat, and 26·0 per cent. fatty acid. The test-meal showed free hydrochloric acid. The red blood-cells were 4,000,000 per c.mm.; hæmoglobin, 68 per cent.; colour-index, 0·85; white blood-cells, 4200 per c.mm.

On June 9th, 1930, she was admitted to the London Hospital complaining of diarrhœa and cramps in the hands and feet. Appetite excellent.

Clinical examination.—Weight 7 st. 2 lb. Height 5 ft. 1¼ in. A pale thin woman, with a dry skin and seborrhœa of the right eyebrow. There was no bone deformity. The Chvostek and Trousseau signs were positive. Slit-lamp examination showed fine scattered opacities throughout the

lens; a few in the fœtal nucleus (Mr. C. Goulden). She was deaf, and examination of the ears showed bilateral adhesive catarrh of both Eustachian tubes with fibrous ankylosis of the left ossicles and two perforations of the left tympanum. The heart and lungs were normal. B.P. 110/70. There was slight distension of the abdomen. The liver was palpable 3 cm. below the costal margin on inspiration.

Special examinations.—Urine normal. Stools pale and porridgy in consistency. Total fat, 75·8 per cent.; unsoaped fat, 67·4 per cent. Serum calcium, 8·4 mg. per 100 c.cm. Plasma phosphorus, 3 mg. per 100 c.cm. Plasma phosphatase, 0·283. Test-meal: free hydrochloric acid, 0·27 per cent.; total acidity, 80. Blood count: red blood-cells, 4,000,000 per c.mm.; hæmoglobin, 62 per cent.; colour-index, 0·76; white blood-cells, 4800 per c.mm.; polymorphs, 67 per cent.; lymphocytes, 24·5 per cent.; eosinophils, 4 per cent.; large mononuclears, 4·5 per cent. Wassermann reaction negative. Urine normal.

Course.—She improved on a low fat, high vitamin diet, together with calcium lactate 10 g. daily.

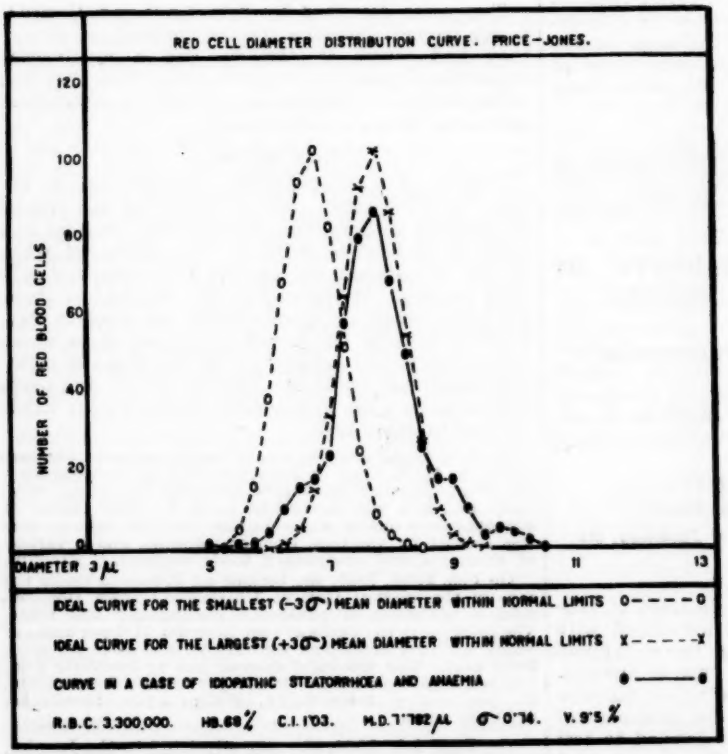
On Jan. 21st, 1931, she was readmitted to the London Hospital complaining of diarrhœa, weakness, dyspnœa, and palpitation.

Clinical examination.—Weight 7 st. 6 lb. Chvostek sign positive. Trousseau sign negative. Slight icteric tinge of conjunctivæ. Tongue smooth, papillæ pale and atrophic. Soft, light brown hair, with a tendency to silver grey. Skin dry. Large moist red abraded areas from 2 cm. to 8 cm. diameter on all limbs, and to a lesser extent on trunk. Many of these lesions showed scaly brown pigmented borders. One lesion on the left calf showed a deep brown scaly periphery and a moist red abraded centre.

Special examinations.—Stools: total fat, 39·8 per cent.; unsoaped fat, 15·6 per cent. No amœbæ or cysts seen in the stools. Agglutination reactions negative for typhoid and dysentery organisms. Blood-urea, 20 mg. per 100 c.cm. Sugar-tolerance test: fasting blood-sugar, 0·064 per cent.; blood-sugar after 50 g. of glucose by mouth—in 45 minutes 0·077 per cent., in two hours 0·08 per cent., no glycosuria throughout. Test-meal: free hydrochloric acid, 0·22 per cent.; total acidity, 80. Serum calcium, 8·4 mg. per 100 c.cm. Plasma phosphorus, 2·1 mg. per 100 c.cm. Calcium balance: the calcium output was estimated in the urine and fæces for three three-day periods. The patient was kept on a weighed diet of known low calcium content. The calcium output in the urine was much less than normal (0·04 g.); that in the fæces was double the normal (0·91 g.). Controlled radiograms revealed no abnormality in the bones examined. Examination by opaque enema showed a condition of megacolon in which four pints of barium sulphate were used, the whole colon being of poor tone and showing great enlargement of the lumen. Blood count: red blood-cells, 1,400,000 per c.mm.; hæmoglobin, 62 per cent.; colour-index, 1; white blood-cells, 3200 per c.mm.; polymorphs, 63 per cent.; lymphocytes, 27 per cent.; eosinophils, 3 per cent.; large mononuclears, 7 per cent.; severe anisocytosis, punctate basophilia, poikilocytosis. Indirect van den Bergh reaction, 0·1 mg. per 100 c.cm.

Course.—There was a rapid response to liver extract therapy, the reticulocytes reaching a level of 18·5 per cent. and the total red cell count 4,300,000 per c.mm. The patient did not take the liver extract regularly, and the anæmia relapsed. She was therefore readmitted for intensive treatment of the anæmia on Dec. 18th, 1931. Blood count: red blood-cells, 3,300,000 per c.mm.; hæmoglobin, 68 per cent.; colour-index, 1·03; white blood-cells, 2400 per c.mm.; polymorphs, 56 per cent.; lymphocytes, 39·5 per cent.; eosinophils, 3 per cent.; large mononuclears, 1·5 per cent.; platelets scanty, anisocytosis, no poikilocytosis, mean diameter of red cells, 7·782 μ; just larger than the largest calculated normal mean of 7·718 μ. The variability was 9·5 per cent. and there was 8·8 per cent. megalocytosis. The Price-Jones curve is shown in Fig. 1. The indirect van den Bergh reaction varied between 0·5 and 0·75 van den Bergh units. Urobilinogen not in excess in the urine

FIG. 1 (Case 1).



TREATMENT.

She was given a high calcium diet which contained meat and green vegetables and, in addition, 12 g. of marmite daily. Radiostol and calcium lactate were discontinued, to obtain as far as possible a pure marmite effect. Daily blood examinations were made. The reticulocytes started to rise on the sixth day, reaching a maximum of 10·8 per cent. on the ninth day, and then falling slowly to normal (Fig. 2). The red blood-cells and hæmoglobin rose steadily, the red blood-cells reaching a level of 4,000,000 per c.mm. 25 days after treatment was begun. They are now, 5,000,000 per c.mm., and the hæmoglobin is constantly in the neighbourhood of 80 per cent., while the indirect van den Bergh reaction is 0·25 van den Bergh units. The diarrhœa and tetany which previously had been controlled became extremely severe after radiostol and calcium were omitted, but despite this there was a gain in weight, and the improvement in the blood picture was no slower than in Case 2, where diarrhœa was not severe. The significance of this observation is discussed later.

CASE 2.—A single woman of 22 years, seen in consultation with Dr. D. S. Campbell, of Grimsby.

Clinical history.—She was an only child, and since babyhood had always had loose stools. They were pale, but not bulky or offensive. No blood or mucus was ever passed. She never had the energy to play games. Three years ago she began having attacks of diarrhœa every two weeks, when she passed as many as eight motions a day. She does not dare to drink hot food for fear of precipitating an attack. Unrelated to the diarrhœa she gets tingling and numbness

in the fingers, and in some attacks the thumb gets stiff and tucked into the palm. Such attacks are very awkward, and have interfered with her study of music, especially playing the piano.

Clinical examination (May 6th, 1931).—Weight 7 st. 4 lb. Height 5 ft. 1 in. Pale skin and mucous membranes, slight malar flush. There was no bone deformity. Small adenoma, 2 cm. diameter, in isthmus of thyroid. Chvostek sign negative. Trousseau sign positive. Heart and lungs normal. Blood pressure 130/90. Moderate distension of abdomen, no tenderness.

Special examinations.—Urine normal. Stools: pale, porridgy; total fat, 35·6 per cent.; unsoaped fat, 16·5 per cent. no occult blood. Test-meal: free HCl, 0·16 per cent.; total acidity, 66. Serum calcium, 7·9 mg. per 100 c.cm. Plasma phosphorus, 2·5 mg. per 100 c.cm. Calcium balance: the calcium output was estimated in the urine for three three-day periods. The patient was kept on a weighed diet of known low calcium content. The calcium output in the urine was much less than in the normal (0·03 g.) Radiograms of bones: a controlled radiogram of the right hand showed a slight uniform diminution of calcification (Dr. Stephen Montgomery). Blood count: red blood-cells, 2,500,000 per c.mm.; hæmoglobin, 55 per cent.; colour-index, 1·1; white blood-cells, 4400 per c.mm.; polymorphs, 30 per cent.; lymphocytes, 66 per cent.; eosinophils, 1 per cent.; large mononuclears, 3 per cent. Wassermann reaction negative.

Progress under treatment.—She was given a low fat, high calcium diet, with the addition of calcium lactate (10 g.) and two tablets of Radiostol (British Drug Houses) daily. There was immediate improvement of the diarrhœa, and she began to pass only two stools a day. The tetany disappeared. Iron in large doses was given, but the anæmia remained unaltered for six months.

On Dec. 29th, 1931, she was admitted to a nursing home for intensive treatment of the anæmia.

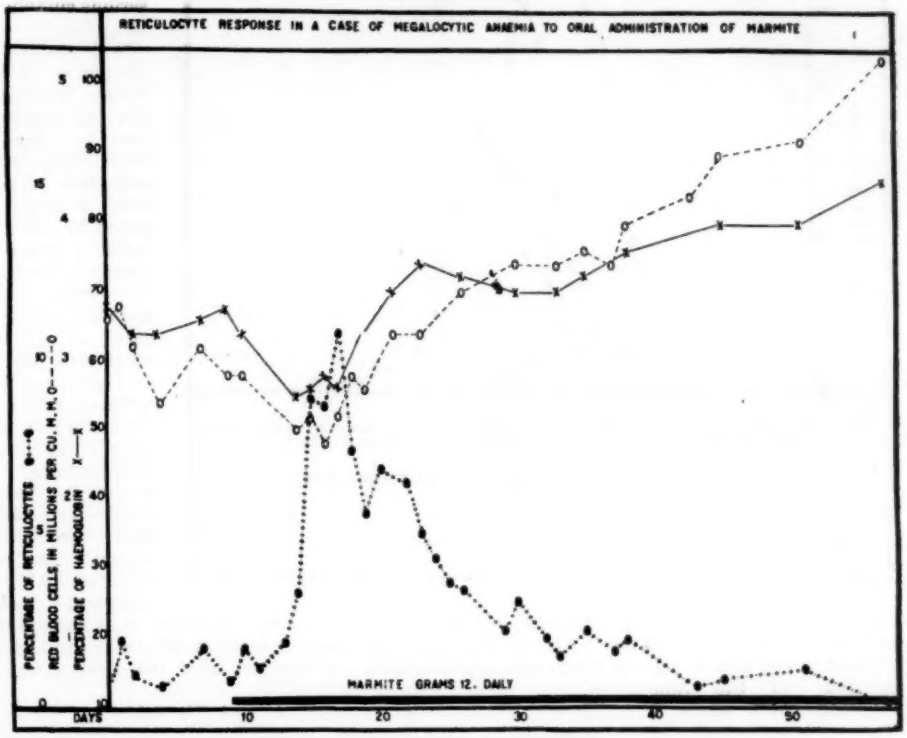
Clinical examination.—Weight 6 st. 13 lb. Pale skin with malar flush and slight icteric tinge of conjunctivæ. Tongue raw with red edges. (To a direct question she answered that her tongue had often been sore.)

Special examinations.—Stools: total fat, 18·7 per cent.; unsoaped fat, 11·8 per cent. Sugar-tolerance test: fasting blood-sugar, 0·054 per cent.; blood-sugar after 50 g. glucose by mouth—in 40 minutes 0·076 per cent., in 80 minutes 0·075 per cent., in two hours 0·083 per cent., no glycosuria throughout. Serum calcium, 9·7 per mg. per 100 c.cm. Plasma phosphorus, 3·5 mg. per 100 c.cm. Plasma phosphatase, 0·182. Blood count: red blood-cells, 2,500,000 per c.mm.; hæmoglobin, 52 per cent.; colour-index, 1·04; white blood-cells, 2400 per c.mm.; polymorphs, 39 per cent.; lymphocytes, 58 per cent.; eosinophils, 1 per cent.; large mononuclears, 2 per cent.; reticulocytes, 1·7 per cent.; platelets scanty, great anisocytosis, no poikilocytosis. The mean diameter of the red blood-cells was 8·115 μ, the variability 11·7 per cent, and there was a megalocytosis of 37·2 per cent. giving a curve compatible with a diagnosis of pernicious anæmia (Fig. 3). The indirect van den Bergh reaction was 0·75 van den Bergh units.

TREATMENT.

In order to simplify the conditions of the experiment as far as possible during the initial period the patient was given no red meat, and no fresh fruit or green vegetables. Chicken once a day was allowed. To this was added 12 g. of marmite, usually taken cold. This was much disliked at first, but was soon tolerated. Daily blood observations were made. The reticulocytes started to rise on the sixth day, reaching a maximum of 17·2 per cent. on the eleventh day, and then falling slowly to normal. This was followed by a rapid rise in both red blood-cells and hæmoglobin (Fig. 4). Thirty-nine days later the red blood-cells were 4,000,000 per c.mm., hæmoglobin 78 per cent., colour-index 0·9. The indirect van den Bergh reaction was 0·2 van den Bergh units. Progress has continued, and the red blood-cells are now 5,200,000 per c.mm., hæmoglobin 88 per cent., colour-index 0·84. There is still a leucopenia, the white blood-cells being constantly between 2000 and 3000 per c.mm. The striking hæmatological improvement was accompanied, as in Addisonian pernicious anæmia, by an increased sense of well-being and by a gain in weight [29]—1 st. 3 lb. in 10 weeks, in spite of occasional attacks of diarrhœa lasting one to two days.

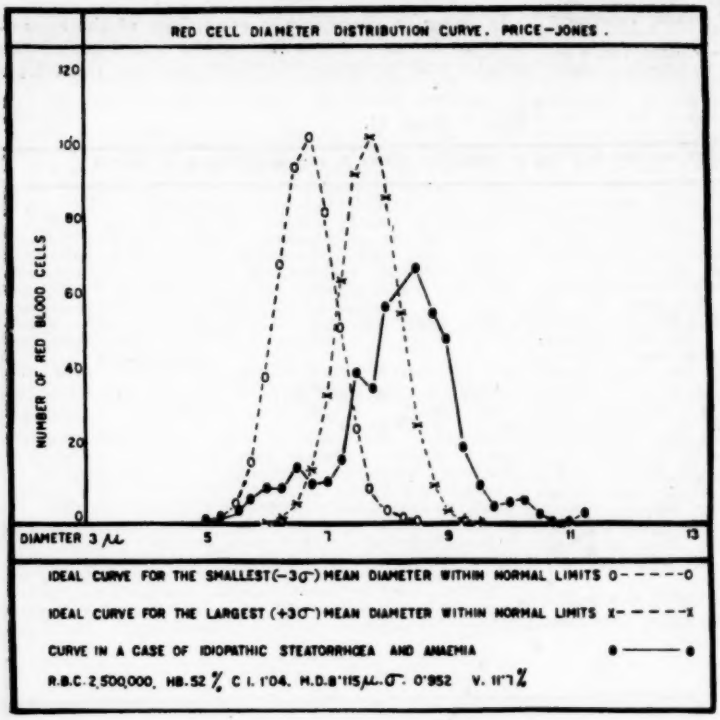
FIG. 2 (Case 1).



CHARACTER OF THE ANÆMIA.

Both cases showed a hyperchromic megalocytic anæmia similar to other reported cases. There was a striking absence of poikilocytosis, as was also noted by Blumgart [2] and Holmes and Starr.[16] The van den Bergh indirect reaction was low, varying between 0·5 and 0·75 van den Bergh units. Holmes and Starr also record a negative reading in the only one of their cases in which the examination was made, and

FIG. 3 (Case 2).



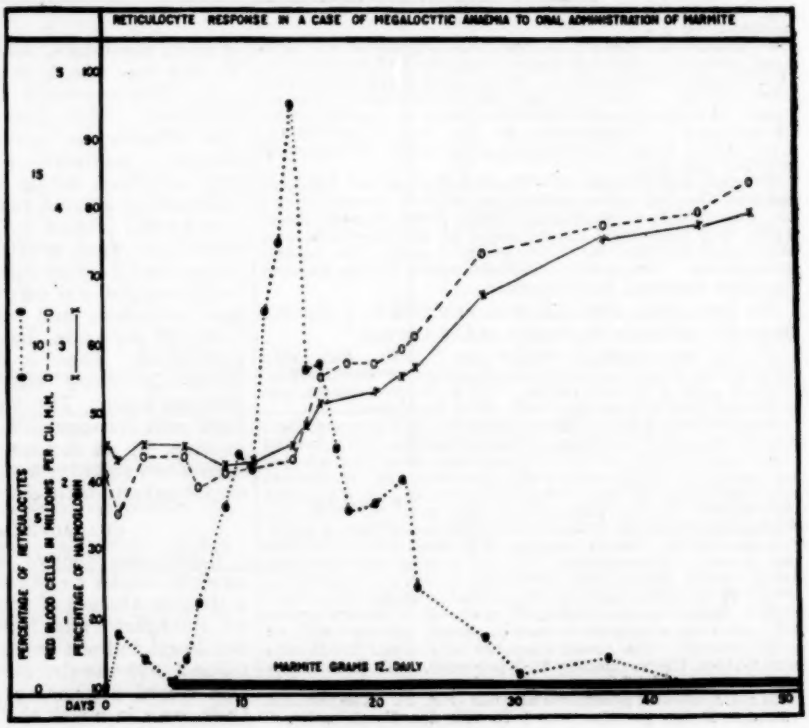
no comment is made except by Vischer [30] upon the presence of jaundice. Free hydrochloric acid was present in the gastric juice in both cases, and occurred in four of the nine reported cases where a fractional test-meal was done. Thaysen [28] believes that changes in the character of the anæmia occurring in the same patient are peculiar to cœliac disease. He, however, makes no attempt to correlate his blood findings with the effect of treatment. It is well known that certain cases of Addisonian anæmia require iron before the blood picture becomes normal, and also that spontaneous remissions occur without any treatment. The most dramatic changes in cœliac disease have been reported in children in association with sepsis, but again sepsis will precipitate a relapse in Addisonian anæmia. The anæmia, therefore, is in no way peculiarly polymorphic.

RESPONSE TO MARMITE.

In both cases the response of the anæmia to marmite was as dramatic as that obtained by the administration of liver extract in the treatment of Addisonian pernicious anæmia. Minot [22] and his associates have shown that in the latter, if maximum amounts of potent material are given, no serious complications being present, the height of the reticulocyte rise is inversely proportional to the level of the red blood-cells before treatment. In both cases the maximum reticulocyte level was in close accord with that calculated, suggesting that an adequate dose was given. In order to study its action uncomplicated by other drugs radiostol and calcium lactate were not given to Case 1. The blood picture returned to normal, and some weight was gained, though both the diarrhœa and tetany were severe until controlled by other means.

Theoretically marmite might exert its action either by favouring the absorption of, or actually supplying, some factor essential to hæmopoiesis. The blood-sugar curve in both cases, however, retained its characteristic flattened form despite recovery from the anæmia, and as long as radiostol was withheld, severe tetany and diarrhœa continued in Case 1. It is clear, therefore, that absorption of other essential substances is unaffected; and, since it is difficult to understand why the absorption of one factor only

FIG. 4 (Case 2).



REPORTED CASES OF MEGALOCYTIC HYPERCHROMIC ANÆMIA ASSOCIATED WITH CŒLIAC DISEASE.

Author.	Age in years.	Sex.	Date.	Red blood-cells (thous. per c.mm.)	Hæmoglobin %.	Colour-index.	White blood-cells per c.mm.	Megalocytosis.	Anisocytosis.	Poikilocytosis.	Indirect van den Bergh reaction.	Test-meal.	Treatment.	Remarks.
Vischer, Hotz, Habliitzel-Weber.	4½	F	—	1140 550	30 10	1·57 1·0	5400 ..	+ ..	+ ..	.. ..	S.sc.	—	Iron. Intramuscular blood.	Bronchitis; p.-m. diag.: pernicious anæmia.
Hotz, Habliitzel-Weber.	9½	F	22/10/22 22/2/23 8/5/23	3900 554 3700	48 8 41	0·61 0·8 0·55	6500 2780 8000	.. + ..	.. + ..	.. + ..	.. .. ..	Free HCl. No free HCl.	Arsenic. Blood transfusion.	Fever: pyelitis.*
Lehndorff and Mautner.	3	F	—	1400 550	30–40 10	.. 1·34	5400 ..	.. +	.. +	.. ..	.. ..	—	—	p.-m. diag.: pernicious anæmia.
Same authors.	1½	—	—	5200 540	55 8	0·52 0·8	.. ..	.. +	.. +	.. ..	.. ..	—	—	Fever; cardiac murmurs. Recov.
Fanconi.	12	M	—	1600 4750	30 74	1·17 0·98	7000 4900	+ −	.. ..	.. ..	.. +	Free HCl.	Iron and arsenic.	—
Blumgart.	42	M	—	2900	65	1·26	5000	+	+	−	..	Free HCl absent.	—	p.-m.; not typical of pernicious anæmia.
,,	32	M	—	2050	60	1·5	3800	+	+	−	..	Free HCl absent.	—	
Holmes and Starr.	34	M	—	1790 4140	59 80	1·5 0·97	5950 6100	++	+	−	..	Free HCl.	Trypsin, diastase, cod-liver oil, yeast, &c.	—
Same authors.	53	F	—	915 4500	30 80	1·6 0·88	2125	++	+	−	−	Free HCl absent.	Liver, fruit, cod-liver oil.	—
Same authors.	54	M	—	2600 4970	53 80	1·0 0·81	3700 6500	+	+	−	..	Free HCl.	Liver, fruit, [cod-liver oil.	—
Hampson and Shackle.	16	F	—	3420	54	0·8	4700	8·51 μ	..	..	+	—	—	—
Holst.	33	F	—	1320	39	1·5	4000	8·5 μ	..	..	+	Free HCl.	—	—
Witts.	62	M	—	2500	55	1·1	3400	+	+	..	..	Free HCl after lavage.	Liver.	Improved.
Thaysen.	43	M	16/8/24 16/8/25 20/1/26	4200 2800 4700	82 86 71	0·9 1·4 0·8	6000 9800 ..	.. + ..	.. + ..	.. .. ..	.. .. ..	—	—	—
,,	58	F	26/2/26 21/10/28 31/10/29	1640 4800 2400	53 81 68	1·6 0·8 1·4	3200 6000 3600	.. .. +	+ .. +	.. .. ..	.. .. ..	—	—	—
,,	49	F	1912 20/5/23 1928	4600 1100 4500	58 30 70	0·6 1·4 0·8	6000 5000 6500	.. + ..	.. + ..	.. + ..	.. .. ..	—	—	—

S.sc. = Subicteric sclerotics. * Blood picture described by Adler as pseudo-pernicious anæmia of children.

should be facilitated, it appears more reasonable to conclude that marmite supplies or enables the body to prepare some principle essential to normal bone-marrow activity. These observations also suggest that marmite exerts its action upon the disordered hæmopoiesis alone, since other symptoms were unaltered.

RELATIONSHIP OF MARMITE TO THE PRINCIPLE IN LIVER EFFECTIVE IN PERNICIOUS ANÆMIA.

Marmite was without effect upon the hypochromic and erythroblastic types of anæmia occurring in association with cœliac disease.[1] Presumably, therefore, it exerts a specific action, as does the effective principle in liver upon some failure of hæmopoiesis resulting in a megalocytic anæmia. Such a statement raises the question of its relationship to this principle.

Case 1 had previously responded to liver extract with complete recovery of her anæmia. Two of the cases reported by Holmes and Starr[16] recovered when whole liver was given in addition to other therapeutic measures. The case reported by Witts[33] also improved on liver extract, which suggests that probably a factor common to both liver extract and marmite is involved. Marmite is a complex substance prepared commercially from yeast. It contains, therefore, all the constituents of the vitamin B complex, and small amounts of such things as celery seeds added for flavouring purposes. Liver extract is also rich in vitamin B.[11] Experimental evidence, however, as to the effect of the vitamin B complex upon hæmopoiesis is conflicting,[12 26 27] whilst clinically anæmia is not invariably associated with either of the conditions due to lack of vitamin B. If anæmia occurs in beri-beri[19] or pellagra,[3] it is almost invariably hypochromic in character.

Marmite, however, is useless in the treatment of Addisonian pernicious anæmia,[6] which suggests that though the substances effective in the treatment of the two anæmias are both present in liver extract they are not identical. It is clear that until further work has been done it is impossible to determine which element in marmite is concerned in hæmopoiesis, and how it is related to the principles in liver extract.

RELATIONSHIP OF THE ANÆMIA TO DIARRHŒA.

Diarrhœa.—Castle[5] and his co-workers in discussing the part played by disorders of the digestive tract in the ætiology of anæmia conclude "in general

it can be shown that patients with diarrhœa are more prone to develop anæmia than patients without diarrhœa." Thus Keefer [20] and his associates have recently found that the various types of anæmia which may be associated with tuberculous and dysenteric ulceration of the intestine improve when the diarrhœa is controlled. Lehndorff and Mautner [21] draw the same conclusion in the case of cœliac disease. A study of the present cases, however, suggests that the failure of hæmopoiesis is not dependent upon a deficiency brought about by loss of essential factors due directly to the diarrhœa, but rather to some associated but independent failure of absorption and digestion. Thus in Case 2 the diarrhœa was controlled for six months but the anæmia persisted until relieved immediately by the administration of marmite; while Case 1 was cured of her anæmia in spite of persistent diarrhœa. Certain cases with severe steatorrhœa, to be reported later,[1] have never shown any anæmia. Castle [6] and his co-workers have shown experimentally that such an associated but independent failure of digestion occurs both in chronic diarrhœa associated with intestinal anastomoses and in sprue.

RESPONSE OF OTHER SYMPTOMS TO MARMITE.

The pellagra-like skin lesions in Case 1 responded as dramatically as the blood picture to the administration of marmite. It is likely that this was due to the rich content of vitamin B_2. All other symptoms were unaffected.

RELATIONSHIP OF THE HYPERCHROMIC MEGALOCYTIC ANÆMIAS OF CŒLIAC DISEASE TO OTHER MEGALOCYTIC ANÆMIAS.

The question at once arises as to the relationship of this type of megalocytic anæmia to Addisonian pernicious anæmia and that occurring in sprue, in association with gastrocolic fistula, and in tropical anæmia. They are all hyperchromic anæmias with a marked shift of their red blood-cell distribution curve to the right of normal. They react to the effective principle in liver extract or its substitutes, and, except for a few atypical cases in children, fail to respond to iron. Addisonian pernicious anæmia differs from the others in the following ways:—

(1) The indirect van den Bergh reaction is always high, readings of from 2·0 to 5·0 van den Bergh units being common during a relapse.[7]

(2) Poikilocytosis is a feature of the stained film.

(3) Free hydrochloric acid is almost invariably absent from the gastric juice.

(4) The anæmia is unaffected by marmite.

In cœliac disease the indirect van den Bergh reaction is low. Similar low readings are recorded in sprue,[7] in tropical megalocytic anæmia,[31] and in anæmia associated with gastrocolic fistula.[8] The slight poikilocytosis of cœliac disease is also a feature of sprue [7] and tropical megalocytic anæmia.[31] Free hydrochloric acid is not infrequently found in all megalocytic anæmias other than Addisonian pernicious anæmia. Marmite has been shown to be effective in two cases associated with cœliac disease and in tropical megalocytic anæmia,[32] while it is valueless in the idiopathic form. It appears, therefore, that there is a large group of megalocytic anæmias, possessing certain features in common, which can be differentiated from Addisonian pernicious anæmia.

SUMMARY.

(1) Two cases of megalocytic hyperchromic anæmia associated with tetany and steatorrhœa are reported. (2) The anæmia was cured by the administration of adequate doses of marmite, the other symptoms being unaffected. (3) The anæmia appears to be unrelated to the severity of the diarrhœa or other symptoms. (4) The relationship of this type of megalocytic anæmia to other megalocytic anæmias is discussed.

It is a pleasure to thank Dr. Price-Jones for his kindness in determining the red blood-cell distribution curves and the physicians of University College Hospital for permission to include abstracts from their notes in Case 1.

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GLASGOW LOCK HOSPITAL.—The annual report shows that in 1931 the average number of patients resident nightly was 72, as against 58 in 1930, while the average sojourn of patients benefited was 64 days, compared with 51 in the preceding year. The dispensary attendances were 19,871, as against 19,919 in 1930. The greater number in residence is attributed not to any increase of disease in the community, but rather to a change of attitude on the part of the persons afflicted, and also on the part of the public. The old feelings of secret fear and open distrust are stated to be giving way to feelings of confidence and hope—and the policy of spreading knowledge which the hospital is pursuing is held to have justified itself.

OPHTHALMIC HOSPITAL OF ST. JOHN IN JERUSALEM. The report for 1931 states that there was a marked increase in the number of in-patients. There were 2911 operations and 75,423 attendances of patients who, however, gave no more than £3 (Palestine) as thank-offerings. Endowments produced only £P925, but the expenditure was £P5,329, the bulk of the difference being provided by the Order of St. John. The hospital has complied fully with the "almost Utopian regulations for the installation of sanitary systems" connected with the municipal water-supply of Jerusalem, but since the gravitation supply is "available only for a few hours every fourth day" the scheme which last year cost the hospital £P104 is "little more than a nuisance." Prices in the city have risen substantially, fresh meat by as much as 12 per cent.

CLINICAL AND LABORATORY NOTES

A CASE OF CEREBRAL TUMOUR.

BY F. CLAYTON, M.D.CAMB., M.R.C.P.LOND.,
HON. PHYSICIAN TO THE WARNEFORD HOSPITAL, LEAMINGTON.

ON July 25th, 1930, A. B., aged 22, was indulging in a day by the sea. He spent a good deal of the day in the water, but even more in sun-bathing on the seashore. In the afternoon he had a sudden attack of pain in the head, severe enough for him to consult a doctor, by whom the diagnosis of "heat-stroke" was made. From this time until admission to the Warneford Hospital six weeks later the headache never left him and it began to be associated with vomiting every morning and at varying times in the day. He also complained of double vision on looking to the right, five days before he came into hospital.

On admission he seemed in great pain, referred chiefly to the back of the head; he was quite sensible and showed no drowsiness. His right pupil was smaller than the left; both reacted to light and accommodation. No nystagmus. Right external rectus muscle weak. Tongue protruded slightly to the right. No facial weakness. No loss of power or loss of sensation in trunk or limbs. Deep reflexes all brisk and equal. Abdominal reflexes present; right lower abdominal definitely diminished. Plantar responses flexor.

Radiography of the skull revealed no abnormality. Ophthalmoscopic examination of the fundus oculi showed papilloedema of both discs, especially on the right side. The ears showed no evidence of anything pointing to intracranial sepsis. The cerebro-spinal fluid was under great pressure; there was no excess of protein, and the cell count was normal. The Wassermann reaction in cerebro-spinal fluid and blood was negative.

On Sept. 10th, 1930, a right subtemporal decompression was performed by Mr. Gordon Dingley. The trephine opening was enlarged to a diameter of three inches and on incising the dura the brain bulged through it under great pressure. The brain was explored but no tumour was discovered and the wound was closed. On the 11th headache and vomiting disappeared. On the 17th the decompressed area was bulging considerably and pulsating freely. No symptoms. On the 26th the patient was discharged with a large "hernia cerebri." There seemed to be some left facial weakness. The mental condition had become rather strange. It was then decided to use radium and on Oct. 13th, 1930, a Columbia paste helmet with 64 mg. was applied. The hernia was very tense at this time. The helmet was worn for 18 hours daily for a fortnight. The total amount was 19,406 mg. hours. On discharge from the hospital there was little change in the size of the tumour.

On Oct. 31st, however, it was softer and smaller, and on Nov. 20th it had disappeared.

From that time the condition of the patient has steadily improved, and he is now able to carry on his ordinary work.

He has no headache and has completely normal vision. The optic discs are clear. The origin of the tumour and its nature are necessarily unknown. From the man's story there seems no doubt that his symptoms resulted from exposure to the sun. Similarly from clinical observation there is reasonable evidence for correlating the application of radium with the subsidence of the tumour.

DIHYDROMORPHINONE HYDROCHLORIDE (DILAUDID).

BY O. LEYTON, M.D. CAMB., D.SC., F.R.C.P. LOND.,
PHYSICIAN TO THE LONDON HOSPITAL.

THIS communication is in no way a clinical study of a comparatively new drug but has for its object its introduction to practitioners in Great Britain.

In THE LANCET of last year (1931, ii., 55) an article appeared entitled "The Heroin Habit" from which I may quote the following:—

"The properties of heroin, which render it popular with some physicians, can in most if not all cases be efficiently replaced by other morphine drugs. For the relief of cough codeine is a valuable substitute, though not so strong as heroin; dicodid has as powerful an effect on the respiratory centre as morphine, though less than that of heroin, and its addiction properties are less pronounced than those of the latter drugs. For the relief of pain in patients in whom it is undesirable to act on the bowels, heroin is better than morphine but dilaudide offers the same advantages. This alkaloid has much the same type of effect on the respiratory centre as heroin but is weaker; it has about the same influence as heroin in its pain-relieving properties, and, like heroin, has little effect on the alimentary canal. Furthermore, the euphoric effects of dilaudide are weaker than those of both morphine and heroin as gauged by withdrawal symptoms."

There was a footnote that Profs. Dixon and Tiffeneau had had no experience of dilaudid.

This article aroused in me the desire to test the action of the drug upon some of my patients who were sorely in need of an analgesic. Since the preparation is a derivative of morphine, it is included in the list of substances controlled by the Dangerous Drugs Act, and therefore licences had to be obtained from the Home Office to permit importation of the drug by the London Hospital and a pharmaceutical chemist. These licences were granted without delay and I have now used the drug in a sufficient number of cases to permit me to arrive at a conclusion about its value as an analgesic but not to decide whether addiction develops.

The first case treated was one of thromboangiitis obliterans accompanied by severe pain which was not controlled by any of the many methods adopted, including injection of muscle extract, and necessitated injections of heroin four-hourly. I was faced with the dilemma and concluded that it was wiser to let a man of 75 develop a heroin habit rather than let him sink rapidly under fiendish torture. Heroin had been increased to gr. 1/6 four-hourly and since it was failing to give relief and a bigger dose of heroin may paralyse the respiratory centre morphine had replaced heroin and gr. ¼ was being given at comparatively short intervals. Dilaudid gr. 1/30 replaced the morphine and gave relief for about four hours. The patient was quite willing that all the doses of morphine should be replaced except that given at 10 P.M. He stated that the dilaudid did not help him to sleep.

This patient had been under morphine and heroin for a comparatively short time. Another case seems to show that dilaudid cannot replace morphine when addiction has developed; for the patient who had a draining abscess of lung, and was taking morphine sulphate up to grs. 30 daily, was given dilaudid without any relief. A third case was that of a hospital nurse who suffered from tic douloureux. An injection of dilaudid relieved pain; it did not cause sleep but left her in a condition which allowed her to carry on her work.

The drug is not completely free from adverse effects, although nausea, when caused, lasts as a rule only a few minutes. One patient, however, a woman of about 60, who was suffering from severe pain due to arthritis deformans, vomited for twelve hours after an injection of dilaudid 0·002 g. This is the only case in which it has caused vomiting.

The drug failed to give relief in a case of what I believed to be "associated pain" or "memory pain."

I have used dilaudid in several dozen cases including pleurisy, sciatica, facial neuralgia, and angina pectoris with beneficial effects. Two cases

which are still under my care have precipitated this communication because I dread to think what their suffering would have been if dilaudid had not providentially come to their aid.

A young man suffering from severe diabetes mellitus developed acute arthritis of his knee, so severe that for a time it was no easy matter to decide that it was not due to osteomyelitis. Excruciating pain persisted for several weeks in spite of the usual analgesics and complete fixation. Dilaudid 0·002 g., to begin with four-hourly and later every six hours, made life bearable. This patient developed distinct euphoria after the injection, but no untoward symptoms have developed on reducing the dose after four weeks' administration of the drug.

The other case is one of actinomycosis of the abdomen. If dilaudid were not available this patient would have had to receive very large doses of morphine which would have led not only to loss of appetite but also to stubborn constipation. The dose in this case had to be 0·004 g. which caused transient nausea and giddiness. The patient's appetite is indirectly stimulated by the drug because he is unable to eat when the pain is severe. Some time before a meal is due he receives a dose which allows him to eat in comfort. In this patient too euphoria follows the injection. The dose has not had to be increased although it has been given for a number of weeks.

In Germany the drug has been given as a rectal suppository with good effects, but of this I have not had experience. From my observations I conclude: (1) unlike morphine, it is not necessary to increase the dose of dilaudid; (2) nausea, giddiness, and confusion may develop for a minute or two, very rarely for longer; (3) the drug does not cause constipation; (4) the appetite is not marred by the drug; (5) in some cases euphoria is induced.

As already stated, I have not used the drug long enough to decide whether addiction develops.

MEDICAL SOCIETIES

ROYAL SOCIETY OF MEDICINE.

SECTIONS OF TROPICAL DISEASES AND OF MEDICINE.

AT a combined meeting of these sections on April 7th the chair was taken by Prof. J. GORDON THOMSON, President of the Section of Tropical Medicine, and a discussion on the

Megalocytic Anæmias of Tropical and Non-tropical Countries

was opened by Dr. L. J. WITTS. Thanks to the work of Dr. Price-Jones, he said, it was possible to construct curves to show whether the cells present in an anæmia were larger or smaller than the normal red blood-cell, or, in other words, to show whether a megalocytic or a microcytic anæmia was present. When megalocytes were present in the peripheral blood there was a proliferation of megaloblasts in the bone-marrow, and this proliferation might be the result of either a megaloblastic degeneration of the bone-marrow—such as that believed to take place in pernicious anæmia and the tropical anæmias—or a hyperplasia designed to repair blood destruction. The anhæmopoietic anæmias fell into three groups: nutritional anæmia, including tropical macrocytic anæmia of pregnancy; gastrogenous anæmia, including pernicious anæmia; and alimentary anæmia, including intestinal anæmia, fatty diarrhœa, and pellagra. Pernicious anæmia was now believed to be essentially due to achylia gastrica; a principle normally formed in the stomach was essential to the development of normal blood, and where this principle was absent it could be replaced by stomach and liver extracts. The intestinal anæmias were often associated with defective diet, achlorhydria, and diminished absorption, and might develop following intestinal resection, or stenosis of the intestine—for example, stenosis due to tuberculosis—infestation with intestinal parasites, and gastro-intestinal ulceration. Fatty diarrhœa was not uncommonly associated with a megalocytic anæmia and was seen in such conditions as cœliac disease, sprue, chylous diarrhœa, pancreatic diarrhœa, and gastro-colic fistula. The anæmia tended to pass through three stages: hypochromic anæmia with normoblastic marrow; megalocytic anæmia with megaloblastic marrow; aplastic anæmia. The first problem in cases of fatty diarrhœa was to decide how far the anæmia was the result of impaired gastric digestion and how far it was the result of diminished intestinal absorption. In a high proportion of cases there was achlorhydria, and in some it had been shown that the gastric intrinsic factor might be absent although hydrochloric acid was present. In some, gastric digestion was normal, and in these the anæmia must be taken as being due to diminished intestinal absorption. In the achylic group the problem was to decide to what extent the anæmia was due to the absence of the gastric intrinsic factor, and to what extent it was due to the absence of the vitamin B complex from the diet.

Megaloblastic proliferation due to an attempt to replace rapidly destroyed blood-cells was an uncommon and obscure condition. In one hæmolytic infection (bartonella) megalocytic anæmia occurred; with syphilis and blackwater fever the anæmia was of the secondary type. A hæmolytic anæmia of pregnancy occasionally occurred in temperate zones and differed from the tropical anæmia of pregnancy. A similar acute hæmolytic anæmia might occur spontaneously in men. Most anæmias of this type were microcytic, but a few megalocytic cases had been described in which there was an increase in the mean diameter of the red cells, but rarely much anisocytosis. A case of aleukæmic leukæmia had been described in which the van den Bergh reaction was positive and megalocytosis, polychromasia, and hæmosiderosis were present, and four cases had been reported by Prof. L. S. P. Davidson in which the red cells as well as the white cells in the blood picture had been affected in patients with Hodgkins disease. He would like to repeat that the two main divisions into which megalocytic anæmias could be grouped were: those due to a megaloblastic degeneration and those due to hæmolysis. Cases in the second group were rare and obscure.

SPRUE.

Dr. N. HAMILTON FAIRLEY said that Oroya fever was the only tropical megalocytic anæmia of hæmolytic origin. The blood destruction was very rapid in this disease and the red cell count might fall to below a million in a few hours. In other diseases, such as blackwater fever, where there was rapid hæmolysis, the bone-marrow always showed an erythroblastic hyperplasia and never a megaloblastic degeneration. The anæmia developing in tropical sprue was megalocytic in a large proportion of cases. The colour-index was usually in the neighbourhood of one, and the red blood count had been between 2 and 3 million at the initial examination in a large series of cases. The patient generally complained of intestinal symptoms.

At one time it had been discussed whether sprue and pernicious anæmia were a single entity. All sprue cases passed through a megalocytic phase unless they were cured before that phase was reached. Cases of sprue treated with liver extract showed a definite and sustained improvement. He described two cases, treated with intravenous Exhepa and Hepatex P.A.F. respectively, which had shown no improvement until given liver extract. Another case of relapsing sprue had improved slightly on exhepa and considerably on hepa simplex, but the mean diameter of the red blood-cells had remained large and the condition had relapsed. A transfusion was given, followed by Ventriculin, but the patient had continued to go downhill. Subsequently there was a marked improvement on hepatex and liver extract, but the patient had since relapsed again and it appeared probable that the anæmia would become aplastic and fail to respond to any form of liver treatment. A fourth case was known to have had hyperacidity in 1925; when seen a few years later, suffering from sprue, he had achlorhydria. The gastric juice, however, showed slight peptic activity, and the condition was not, therefore, achylia gastrica in the full sense. At first there was no rise in acidity following the injection of histamine, but as treatment proceeded a response to histamine developed and later the stomach began to secrete acid spontaneously and in increasing quantities, until a normal curve was established. Tropical sprue was a gastro-intestinal disease characterised by defective gastric secretion and malabsorption of fat, glucose, and calcium in the small intestine. Dysfunction of the small intestine was the essential lesion, and in this sprue differed fundamentally from pernicious anæmia. An additional diagnostic point was that in sprue the rise of blood-sugar in the glucose-tolerance test was delayed, and the delay became less as treatment progressed. In pernicious anæmia the glucose-tolerance test gave a normal curve.

Dr. G. W. GOODHART discussed a series of cases of megalocytic anæmia which could not be classed as pernicious anæmia. He classed them, however, in the group of anæmias due to defective blood formation and not in the group due to excessive blood destruction. They had in common megalocytosis, a high colour-index and leucopenia; all had failed to respond to liver extract, and had appeared to show a certain symmetry in the Price-Jones curve. The first case was clinically a typical pernicious anæmia; there were less than 2 million red cells, the colour-index was high, van den Bergh's reaction positive. There was, however, little anisocytosis though some mégalocytosis. The case did not respond to liver treatment but improved on blood transfusion. When seen later the anæmia was definitely megalocytic in type; the variability was increased. The Arneth count showed a shift to the left: not only was there an absence of the hyper-mature polymorphs typical of pernicious anæmia, but the opposite condition was present—an excess of young forms. At autopsy the bone-marrow was found to be aplastic; he would be interested to know whether pernicious anæmia ever terminated in aplasia. The second case occurred in a girl of 19, who had been complaining of pallor, breathlessness, and attacks of severe abdominal pain and vomiting for 14 months. The van den Bergh reaction was negative; there was no acid in the vomit. She had previously been given liver treatment in St. George's Hospital and while there had passed a melæna stool. The attacks of pain and vomiting persisted in spite of the renewal of liver treatment. The Price-Jones curve showed a shift to the right, variability was increased; there were leucopenia and a shift to the left of the Arneth index. Intestinal obstruction was suspected, but she was too ill for operation. At autopsy there was no bony evidence of pernicious anæmia, but severe ulceration and necrosis, with polypoid masses, were found in the jejunum, and melæna was present throughout the large intestine. Dr. Goodhart referred to seven other cases showing similar blood pictures, one associated with ascites and a contracted liver; another with Hodgkin's disease following prolonged treatment with deep X rays; another with rectal and vaginal hæmorrhages; another, possibly a true pernicious anæmia, associated with chronic intestinal obstruction from tubercular peritonitis; another with a tuberculous cavity in the lungs; another associated with lympho-sarcoma; and another with sprue. All showed a megalocytic anæmia generally with a high colour-index and smaller or greater increase in variability; the Price-Jones curve showed a shift to the right in every case, and appeared to be symmetrical in all except the case with the tubercular cavity in the lungs. The Arneth curve showed either a shift to the left or no change. He had thought at one time that a symmetrical Price-Jones curve might serve to distinguish pernicious anæmia from sprue, but this had not been borne out by experience. He asked whether the curve had been symmetrical in Dr. Fairley's case of sprue which had failed to respond to treatment.

TROPICAL MACROCYTIC ANÆMIA.

Dr. LUCY WILLS said that tropical macrocytic anæmia was seen most commonly in pregnant women, though it also occurred in men and non-pregnant women. Her remarks referred to the disease as seen in India, where it occurred as a rule between October and April, and attacked all communities. Most patients reported for treatment during the second half of pregnancy and if they survived delivery there was generally a rapid improvement, but the death-rate was high, even in treated cases. A satisfactory history regarding fever was hard to obtain; diarrhœa and vomiting had been described as typical by Balfour, but varied with the incidence of diarrhœa in the population; sore tongue was usually present. The anæmia was very severe; in 54 consecutive cases 32 had counts below one million when first seen. The death-rate among her cases had not been much improved by liver extract at first, because the patients reported so late in the disease, but subsequently when the value of marmite was established and when patients began to appear at hospital earlier, the death-rate fell considerably. The blood picture was that of a megalocytic anæmia with a few megaloblasts and normoblasts. The Price-Jones curve showed a shift to the right and increased variability; there were few reticulocytes and the white cell count was variable. There was no hyperbilirubinæmia or other evidence of hæmolysis, and the test-meal showed normal acid secretion. Before the introduction of liver therapy all treatment was useless, but patients could now be treated successfully with liver extract or marmite, a yeast extract. The distribution of the disease, and dietetic surveys, suggested that it was a nutritional disorder. Dr. Wills had found diet grossly defective throughout the city in a survey she had made in Bombay. Marmite was inactive in Addison's anæmia so that the curative factor could

not be Cohn's anti-anæmia factor but was possibly some part of the vitamin B complex, though the evidence was not conclusive that this was so. She had been able to produce a similar anæmia in monkeys by feeding them on diets based on the diet prevalent among the hospital class of patient, and deficient in vitamins, proteins, and salts. The condition ended fatally, but in a few cases which were preserved subsequent feeding with marmite proved to be curative. Marmite was a source of vitamins B1 and B2, but experimental work, and the freedom of beri-beri patients from this anæmia would seem to exclude B1 deficiency as the causative factor; more work was necessary to determine the exact nature of the active fraction. She asked whether Dr. Fairley had tried marmite in the treatment of sprue, as good results had been reported from its use in Madras.

Dr. C. PRICE-JONES said that the chief importance of his curves was to estimate anisocytosis. Their second advantage lay in the fact that from the distribution of cells the mean cell diameter could be calculated; this had no correlation with the degree of anisocytosis, but the variability had, and was therefore important. In the third place the curves showed the relation of distribution of cells and of their mean diameter to those of normal blood, as calculated from the examination of 50,000 normal cells. The appearance of symmetry in a curve could not be accepted as its face value; it was rash to call a curve symmetrical unless a mathematical calculation had been made to decide the degree of symmetry. The variability was much more important than the mean diameter; in cases other than pernicious anæmia the variability was low. In dysfunction of the bone-marrow there was megalocytosis and extreme variability, but where all the cells were affected, for example, by a toxin, the variability was not affected and might be low.

Prof. M. J. STEWART (Leeds) mentioned some cases of trinitrotoluene poisoning seen during the war. The blood changes in these had usually been aplastic, but in one or two cases they were megaloblastic. In one girl of 18 with atrophy of the liver there had been repeated showers of megaloblasts into the blood; she had made a good recovery. He wondered whether the case of megalocytic anæmia associated with contracted liver, mentioned by Dr. Goodhart, might possibly have been a case of necrosis of the liver.

Dr. R. C. LIGHTWOOD said that pernicious anæmia was almost unknown in children though recently a few cases had been reported. There might be three reasons for this; possibly the stomach might be more effective in producing the factor which stimulated the bone-marrow, but this was unlikely as hypochlorhydria was quite frequently found in children; secondly, pernicious anæmia might depend on faulty absorption of this factor, in which case cœliac disease might be expected to produce pernicious anæmia; thirdly, there might be some difference in the bone-marrow of children, and certainly the marrow was normally more active throughout childhood. Among 39 cases of cœliac disease, three had been quoted as showing the blood picture of pernicious anæmia. The usual blood changes in this condition included secondary anæmia with a low colour-index and a high proportion of lymphocytes. The lymphocytosis was rather characteristic of the disease and very persistent, sometimes being present years after the patient had recovered.

Dr. JANET VAUGHAN referred to 13 cases of cœliac disease treated with marmite. These are mentioned in an original article on p. 829.

In replying, Dr. FAIRLEY said that the curves in sprue had an appearance of symmetry more marked than that of pernicious anæmia curves, but that he would hesitate to regard them as more symmetrical without further calculations. He had not yet made use of marmite in sufficient doses in sprue to have formed any conclusions about its effects.

PADDINGTON MEDICAL SOCIETY.

A MEETING of this society held on April 12th, under the presidency of Dr. SWIETOCHOWSKI, was devoted to a discussion on

A State Medical Service.

Mr. SOMERVILLE HASTINGS said his wish was that everybody, without consideration of ability to pay, should receive in illness the best attention which medical science could give; he also wanted to see more prevention in medical arrangements. He was not advocating the scheme put forward two years ago by the British Medical Association, though it might constitute a useful step in the right direction. His aim was a State service complete, unified, and free. He would have no compulsion for patient or doctor; he wanted a service so good that people would readily avail themselves of it. The doctor would be given freedom in medical matters; his routine clerical work would be done for him. Such a scheme should appeal to the most socialistic of all the professions, for, he said, doctors more than any others practised socialism. Their discoveries were, by tradition, broadcast to the world, and their charges were made according to the means of the patients. A desirable extension of the latter principle was that people should pay for medical services not in hard cash, but in rates and taxes, which were based upon individual means. During the last 50 years the general practitioner had been continuously robbed of clinical material and of interest in his work. Though he might diagnose infectious disease, the treatment was carried out at a fever hospital. Successive enactments had taken away from the general practitioner the diagnosis of one group of cases after another: tuberculosis he now saw less of than formerly, venereal diseases were treated largely in the clinics, and the treatment of school-children had been taken from him; there were also maternity and child welfare centres. In 1927 the *British Medical Journal* said: "There are no fewer than 17 departments, spheres, or directions of clinical activity for which provision is made in this sectional way under the auspices of local authorities; some of these cover an extensive field of medicine." Further, as soon as a patient got into a hospital the general practitioner lost all contact with him. Such were the complications of disease that many more cases were now going into hospitals than formerly, and many of the hospitals were now charging fees. Municipal hospitals were developing side by side with the voluntary hospitals; and because they had the financial backing of the State, and often controlled a bigger area, and so could arrange their clinical material in the way they desired, they were developing into formidable rivals to the voluntary hospitals. The process of providing medical needs by coöperative methods would go on and increase. A strong case could be made out for the treatment of the pre-school child, for the treatment of the adolescent before he came under National Health Insurance, and also for the treatment of all sorts of diseases in special clinics: rheumatism,

orthopædics, heart disease in children, even cancer. He looked upon this kind of thing with serious misgivings, for the State was providing a series of watertight compartments; if the right sort of patient with the right sort of disease fell into the right compartment, he was treated well, but there was little to guide him there. What was needed at the present time was increasing coördination of medical practice—especially at the periphery. It was a disaster to exclude the practitioner from many of the schemes in the profession; for the sake both of the profession and the public a complete State medical service should be developed. In the past, much research work had been done in the big voluntary hospitals; this was not because the staffs of these hospitals had a different type of mentality, but because the conditions of work there were favourable. The profession would produce better results in research if it were unified.

It was unfortunate that the doctor was financially dependent on the patient; if he went to see a patient too often (in the patient's opinion), he was adjudged to want money; if he did not go often enough he was charged with being neglectful. It would make for better work if the doctor could speak freely to the patient without fear that as a consequence he would go to another doctor.

Some form of State service Mr. Hastings regarded as inevitable. Two courses were open to the profession: it could wait and do nothing, and then the politicians would suddenly wake up and would inflict some incomplete and undigested scheme, like the panel or something worse; or it could see what was coming and try to mould public opinion, so that when the change did come a service would be formed which would be advantageous both to the science of medicine and to the public generally.

Sir ERNEST GRAHAM-LITTLE, M.P., recalled a meeting of the society two years ago when he had been asked to open a discussion on the relative advantages of contract and private practice. At that date a scheme for the absorption of the community in contract practice had been put forward by the British Medical Association to forestall, if possible, another scheme which it was feared the Socialist Government intended to rush through. For himself he saw little difference between the two schemes. The B.M.A. scheme envisaged an extension of contract practice which was to include the whole community. Mr. Hastings had not made it clear what sort of general practitioner the socialist scheme had in mind. Did it contemplate a continuance of panel practice or something different? What made the scheme more actual two years ago was the fact that the Socialist Government was in power; that was now no longer the case, and he did not think the danger was likely to be revived in the present generation. The proposals as he saw them were twofold: the part to be played by the general practitioner, and by the hospitals as medical service. Both were to be carefully looked into. Numerically medical men and women were a small section of the community; they could not settle matters in the way they would like; they had to make them acceptable to their masters, the public. Under the proposal just outlined the choice of doctor and of where to go for his treatment were taken from the patient; but the British public could not be forced to go where they did not want to go. In the past the poor-law hospitals—much older as they were than the voluntary hospitals—had never been able to earn anything like their popularity.

But was the medical profession as a body, he asked, so keen upon being converted into a body which would closely approximate to the position of civil servants—i.e., with whole-time medical officers under complete departmental control. If not, he did not think a State medical service was inevitable. To the question, Would it be to the advantage and for the progress of medicine? he would answer emphatically No. Nothing would so conduce to standardisation, for a State possessed neither soul nor mind. In a recent letter addressed to him a young practitioner remarked that the ideal of the Ministry of Health was the practitioner who kept prescribing down and records up. Was such the final aim of the Hippocratic art? Loss of independence and of competition would be a serious drawback in State schemes. Anyhow the cost would be prohibitive; no Chancellor for a long time to come would ask for an additional eleven millions of money. What then was the great advantage of the voluntary hospital system? Mr. Hastings admitted that most of the research had been done there. What distinguished them from State-controlled institutions? First, individual management. In London there were over 100 hospitals belonging to the old poor-law service, now transferred to the London County Council, the affairs of which were managed by a central committee of the council, few of whom could know much about the matters they controlled. Compare therewith last year's work at Charing Cross Hospital, a splendid vindication in the face of great financial stress. How long would it take a municipal hospital to bring about such new additions? Economy would not be secured by handing over private concerns to Government management; a business which became too big for personal attention went to pieces.

DISCUSSION.

Dr. G. C. ANDERSON (deputy medical secretary, B.M.A.) said he did not agree with either opener, though he went further with Mr. Hastings than with his opponent, because now that the State had provided a medical service for the country he felt sure it would be extended. The B.M.A. did not sketch out its scheme because it thought the Labour Government would bring in a State-salaried service; what it was then afraid of, and was still fearing, was that the medical service in this country might develop on wrong lines—that there would be an extension of the clinic system rather than of the panel system. He agreed that at present the general practitioner was being frozen out. For £1,500,000, which might be contributed by the insured persons themselves, a specialist service could be provided from which insured persons were entitled to benefit. He wished the general practitioner to have further opportunities of extending his knowledge by being taken into close association with hospitals in his area. The B.M.A. had attempted to make insurance practice approximate as closely as possible to private practice; that was, he believed, in the interests of the profession and of the community. The present panel system was infinitely better than the service existing previously. He was anxious to prevent practitioners getting into watertight compartments—i.e., attending clinics for one particular disease only. The profession required a wider outlook.

Dr. A. WELPLY (secretary, Medical Practitioners' Union) said the State had stepped in and this movement was sure to progress, whatever doctors might do. He would not exclude people who could afford to pay for their medical attendance; he would

take in every person, irrespective of income. The scheme would naturally embrace 88 per cent. of patients, and legislation for the remaining 12 per cent. would cost a large amount of money, which would be saved by making the scheme all-inclusive. Even under a State service there would still be the private doctor, who would still be able to earn a living. Mention had been made of wastage in municipal hospitals, but he questioned whether there was more waste in them than in voluntary hospitals, which he had long thought employed the most wasteful machinery he had ever seen.

Dr. C. L. BATTESON (secretary, London Panel Committee) said he was opposed to a State medical service, for he thought it neither good for the community nor for the doctor. It was not necessary at the present time to provide full treatment for everybody. He did not think a State service was likely to come in the next 20 years. The only advantage to the public would be that of receiving treatment without making a direct payment. Moreover, under a State service the private practitioner would be gradually squeezed out. Dr. Batteson could not imagine a State service in which there would be any amount of free choice; and such a service would tend to stereotype the work of the profession and to stifle initiative. Also under a State service he did not think salaries would be princely. The price which would have to be paid for the loss of liberty and freedom of action would be too great.

Mr. W. MCADAM ECCLES agreed that service as good as that in the voluntary hospital should be at the disposal of everyone, but he did not agree it was necessary that this service should be under the State. It was difficult to define exactly what was meant by a voluntary hospital, because, so far as the staff was concerned, there was not now the voluntary service that there was 25 to 30 years ago; at St. Bartholomew's the staff had long ceased to be voluntary, for its members were salaried and dismissable at the end of any year. The most important feature of the voluntary hospital was its elastic administration. Moreover, the municipal hospital was only supposed to serve the people in the area of its own administration; and a further important point was the consultative nature of the voluntary hospitals. In this respect at present the municipal hospital was not as perfect as it might be.

Dr. A. BALDIE said that the matter was one of social tendencies—not of party politics or professional prejudice. The tendency to be always looking to the State for support was one fraught with danger to the State, the profession, and the public.

Dr. GERALD SLOT pointed out that in London there were 15,000 voluntary hospital beds, and 80,000 beds in municipal hospitals for the accommodation of the sick poor of London; hence it could be said that the municipal hospitals were doing the bulk of the treatment. People going to the voluntary hospital were seldom seen more than once by the same doctor or surgeon.

Dr. W. G. BENDLE laid stress on the need for giving the practitioner more clinical interest. Much of the treatment in voluntary hospitals was given by very junior men, though theoretically under supervision; the standard of qualification of the staffs of municipal hospitals was relatively higher because they were required to have filled a number of previous posts.

Other speakers were Drs. GIBSON, MELLOTT, STUNGO, FENTON, GRAY, and COHEN, and both openers briefly replied.

NEW INVENTIONS

A NEW TONSIL ABSCESS FORCEPS.

THE instrument here illustrated is designed for the opening of quinseys, and has the following advantages: (1) the point is sharp so that it perforates the overlying tissues easily and comparatively painlessly; (2) the edges passing down to the flange are sharp, though not razor sharp, thus cutting rather

than tearing the tissues when the forceps is opened; (3) there is a flange which takes the place of the old-fashioned strapping wrapped around a scalpel to prevent a too deep penetration; and (4) the shaft is slightly curved so that the hand does not interfere in the line of vision.

The instrument, which has been made for me by Messrs. Allen and Hanburys, of Bethnal Green, London, has proved itself simple, satisfactory, and relatively painless in use.

E. MILES ATKINSON, M.B., F.R.C.S.

BIOPSY AND SKIN GRAFT FORCEPS.

THE purpose of this instrument is to remove small skin strips for grafting chronic ulcers of the legs or ulcers due to burns by burying seeds or strips below the granulations. This small operation is generally done without assistance in the out-patient department, and is accomplished expeditiously and bloodlessly with the help of these forceps. The area from which the skin is to be removed is

first anæsthetised by infiltration, three hypodermic needles (No. 16 or 23 s.w.g.) are then passed through as shown in the illustration. The strip of skin is now pinched up and steadied with the forceps passed underneath the needles, and can be shaved off with scalpel or scissors, all oozing being controlled by the pressure of the forceps. The wound is conveniently closed by threading fine silkworm gut or horsehair through the hypodermic needles before withdrawing them. The forceps resemble ordinary sinus forceps except that a rather long ratchet is incorporated in the handle. In addition to the ordinary uses to which sinus forceps are put, the instrument is useful for holding the vein on the stretch in the operation of ligation of a varicose vein through a small incision. The removal of small skin tumours and of samples of skin for biopsy is much facilitated by using this instrument.

The instrument has been made for me by Messrs. Down Bros., Ltd., St. Thomas's-street, London, S.E.

A. DICKSON WRIGHT, M.S., F.R.C.S.

REVIEWS AND NOTICES OF BOOKS

What Life Should Mean To You.

By ALFRED ADLER. Edited by ALAN PORTER. London: George Allen and Unwin, Ltd. 1932. Pp. 300. 10*s.* 6*d.*

THE tale of literature devoted to Individual Psychology—the theory and practice of Dr. Adler and his friends—grows apace. Dr. Adler's own contributions, during the last few years, have been more than considerable, and may perhaps not unfairly be said to be, in form and quality, at once as baffling, as disarming, and as easily misjudged as is his personality.

Briefly put, Dr. Adler's published works fall into several groups which deserve to be distinguished, the one from the other. The first of these includes the "Organ-Inferiority," the "Neurotic Constitution," and the "Individual Psychology": books written in a not too easily understood German, and for the most part translated none too well, into an even less easily understood English (we had almost said, and perhaps with justice, American) between 1914 and 1924. The successive appearances of these books—some of them collections of essays—marked stages in the development of Individual Psychology, in the technical and scientific sense. In them the fundamental theses of organ-inferiority, the inferiority-sense, the prototype, the neurotic compensation, organ-jargon, and so on, were expounded in close technical terminology and were brought into relation with the classical psychological syndromes or reaction-types as illustrated by case-histories. These works remain indispensable for the professed adherent to Individual Psychology, and for the student of Comparative Psychology.

The books making up the second group (or, marking a second period) are perhaps rather hastily constructed volumes, of American provenance, easily read and pleasant, but discursive, and even formless, consisting in the main of the material from lectures and talks, taken down at the time, and revised for publication by friends and pupils. Among these must be reckoned the "Science of Living," "Understanding Human Nature," and the "Pattern of Life." They are frankly written in terms to be "understanded of the people," and are not necessarily the worse for that. Their engaging simplicity, their naïveté, and the apparent banality of some passages (in spite of the flashes of devastating epigram with which they are brightened) have led to their being under-rated in the mouths of many who confuse dullness with profundity, and simplicity with stupidity. And this, in its turn, has naturally led to a belittlement of Individual Psychology as a serious discipline. But the error of these fallible critics is that of those who have deemed "Alice in Wonderland" merely comic.

In a third and smaller group of volumes, Adler during the last few years has reinforced the links between Individual Psychology and the clinic. In "Problems of Neurosis," and again in the "Case of Miss R.," he has discussed the definite clinical problems of psychoneurosis, of obsession, and the like, in a truly Socratic fashion that is of the utmost help to practising psychologists as well as to many patients. In the present volume, however, a different note is struck. We may surmise that the substance was originally delivered in lecture form—perhaps in America where it was first published—but we are told that it has been edited by Alan Porter, and it is not difficult to recognise the skilled Oxonian hand of the poet, psychologist, and man of letters that we know him to be. The result is that, in despite of a title that is too journalistic, we have a really complete and almost systematic setting out, for the first time, and in agreeable literary form, of the general position taken up by Dr. Adler. The old doctrines that lie at the foundation of his recent constructive thought have been restated, and there is due insistence on recognition by the physician, the pedagogue, and the philanthropist alike, of the need for *coöperation*, in the social as well as in other fields. The orderly arrangement of the chapters, and the gently progressive method of exposition adopted, make this book an admirable one for perusal by the uninstructed practitioner, who will find benefit in a rapid conspectus before proceeding to closer study, and who wishes to recommend a book to his friends and patients. But, this being said, it still is true that, for those who desire really intimate acquaintance with the technique of Individual Psychological Practice, with the special attitude of Individual Psychology towards the sexual problem, and with the full metaphysical and philosophical implications of the whole theory, recourse must be had to the English versions of the three admirable treatises by Erwin Wexberg, of Vienna, and to the smaller books by Philippe Mairet and other English Individual Psychologists.

That Individual Psychology has "come to stay" will hardly, we think, now be disputed. Dr. Ernest Jones has recently admitted that it constitutes perhaps the best, if, indeed, not the only scheme of psychology available for the general practitioner. It is true that he added that this is perhaps less flattering to the medical profession than some might wish it to be. But the admission is important. It was recently said that Individual Psychology stands towards Freudian Psycho-Analysis much as does aseptic surgery towards the old Listerian system, with its paraphernalia of carbolic putty and steam sprays. The analogy may be pressed. Asepsis is now as integral a part of surgery as the disciples of Adler hope that Individual Psychology will come to be in medicine. Like asepsis, too, Individual Psychology is exposed to disparagement. The one was despised as "mere cleanliness"; the other is sometimes contemned as "mere common sense." But, if clean and common sense, why not? Cleanliness and common sense are each of the greatest pragmatic value and are justified alike by the deepest philosophy and the highest science! Again, asepsis and Individual Psychology are subject to like dangers. Insistence on ritual may crystallise into inelastic formalism; but neglect may slide into sloppiness or positive harm. So, at present, Individual Psychology is compelled to face, on the one hand the Scylla of academics, so dreaded by Nietzsche, and, on the other, that Charybdis of refusal to organise and to coöperate which drew Nietzsche to his solipsistic end. The essence of Individual Psychology lies in its freedom to *adapt*. As Einstein has said, it is the psychology of relativity. It has certainly brought relativity into the psychological field. Now, a psychology which can claim the author of the Special and General Theories of Relativity among its adherents can hardly be dismissed so lightly as may think some of those who chuckle over, without understanding, his own

bon mot: that Adler is the Sancho Panza to Freud's Don Quixote.

We commend this book heartily, but as a beginning and not as an end of studies in Individual Psychology.

F. G. C.

Nutrition and Physical Fitness.

By L. JEAN BOGERT, Ph.D., Formerly Instructor in Medicine, University of Chicago. London: W. B. Saunders Co., Ltd. 1931. Pp. 554. 14*s*.

THE arrangement of material in this volume is unusual. The reader is first introduced to a study of the characteristics of the common foodstuffs and the food requirements of the human being; the physiological processes connected with the absorption and metabolism of foods and the disposal of waste material are then dealt with; and finally, the methods of dietary planning are explained as they affect human beings of all ages, including those in normal health and those suffering from various disturbances of nutrition. The author provides a great deal of useful information and displays a worthy restraint in the handling of his material. The language is not technical and suggests that the lay public is the target at which the book is aimed. The average Englishman might benefit considerably by putting into practice the principles of nutrition upon which emphasis is laid, although it is doubtful whether he could easily be persuaded to read the whole of this useful work.

The Search for Man's Ancestors.

By Prof. G. ELLIOT SMITH, M.A., M.D., D.Sc., Litt.D., F.R.S. No. 16, The Forum Series. London: Watts and Co. 1932. Pp. 56. 1*s*.

THIS little book, the latest of a series of monographs by various authorities, is, like the others, a wonderful shillingsworth. Prof. Elliot Smith's name on the title page makes the detailed facts stand beyond question, but the interest is carried further than the actual specimens concerned. These, it might almost be said, are incidental in the story, for he has never lost sight of the object of the book, which is to give the narrative of the how and why of the several findings. It seems incredible that one should sally forth on the face of the earth to some chosen spot, where one has assumed that somebody may have lived and died about half a million years ago, more or less, that one should then dig or delve there with the intention of finding his remains—and that one should find them. Yet something like this has taken place, and these old proto-human fossils have been brought to light. Those who wish to gain some idea of how this has been done cannot do better than buy this booklet; they will not regret the purchase.

Transactions of the American Association of Genito-Urinary Surgeons.

THIS volume (XXIV., 1931) opens with two accounts of Solitary Cysts of the Kidney, a condition that was previously regarded as rare but now seems to be commoner than has been suspected. The first description treats of cysts into which extensive hæmorrhages have taken place, the second of old cysts whose walls have become calcified. In most cases of this sort there is a clear history of previous injury, and Dr. J. A. C. Colston expresses the opinion that wherever there is reason to suspect trauma of the kidney it should be explored. Hæmatomata can then be dealt with, and the risk of transformation into a cyst with subsequent adhesions and calcification can be eliminated.—Drs. D. W. MacKenzie and Allan B. Hawthorne discuss the rare condition of Hæmangioma of the Kidney, and report two cases.—Dr. F. R. Hagner deals with Angioneurotic Hæmaturia. He believes that if these cases are followed to their end many of the patients will be found to die of cardiovascular lesions associated with nephritis.—Drs. H. Cabot and W. W. Holland enter a plea for the more frequent use of nephrostomy, either as a temporary measure to tide over a crisis, or as a permanent remedy for an incurable condition. They describe the technique which they have employed, which is a modification of that advocated by Marion.—Dr. J. I. Farrell has studied the secretion of the prostatic gland in dogs by making a prostatic fistula.—The volume also contains many other interesting papers.

British Journal of Children's Diseases.

To the January–March number Dr. George W. Bray contributes a paper on the Allergic Child, in which he first discusses hereditary disposition which can be demonstrated in from half to two-thirds of all cases, and then the acquisition of sensitisation in those cases in which no definite hereditary influence can be detected. The common characteristics of allergic conditions are described, as well as the common individual manifestations of allergy in childhood, of which the most frequent are cutaneous eruptions such as eczema, flexural pruritus, urticaria and purpura, abdominal conditions, such as food upsets, colic, and recurrent vomiting, hay-fever, migraine, enuresis, and reactions to therapeutic sera and physical agents.—In their paper on Examples of Anæmia of Various Kinds in Children, Dr. F. Parkes Weber and Dr. E. Schwarz describe examples of the following different types of anæmia: (1) severe anæmia cases of agranulocytic or aplastic type which turn out to be really of the nature of lymphatic leukæmia; (2) recurrent epistaxis with anæmia and temporary slight splenomegaly; (3) temporary anæmia probably due to lead; (4) anæmia associated with signs of colitis and enlargement of the liver; (5) severe secondary or chlorotic type of anæmia, probably of nutritional or dietetic origin; and (6) Lederer's acute hæmolytic anæmia.—In a paper on Chronic Streptococcal Toxæmia, Dr. J. D. Hindley-Smith, who reports six illustrative cases, states that this condition is far more widespread than is at present recognised, and appears to be on the increase, especially in large centres of civilisation, so as to be almost as great a menace to national health and economics as tuberculosis. Three distinct stages may be described—viz., a primary in which there is an infected local lesion; a secondary, characterised by general disturbance of the organism; and a tertiary, in which localised damage takes place owing to the defensive reactions of the tissues.—In paper on the Treatment of Early Cases of Knock-knee and Bow-leg in Children, Dr. Edgar Cyriax shows that some of these deformities are primarily due to loss of equilibrium between certain groups of muscles in the thighs, which cause faulty attitudes of the legs, and that early cases can be cured by mechano-therapeutics to restore the loss of balance. In early knock-knee treatment should consist in re-education. Recourse is to be had to the so-called resisted exercises applied according to the Swedish system of Ling, followed by stimulatory *pétrissage* to the weakened muscles, the others being left alone. In bow-leg the weakened adductors of the thigh should be similarly re-educated by means of resisted exercises and subjected to stimulatory *pétrissage*.—Dr. W. R. Bett reports an unusual case of multiple lipomata in a boy aged 2 years, which was successfully treated by operation.—The abstracts from current literature are devoted to diseases of the blood and spleen.

THE LANCET.

LONDON: SATURDAY, APRIL 16, 1932.

VISIBLE "ULTRAMICROSCOPIC" VIRUSES.

THE conception of a visible filtrable virus is no new one. Twenty-eight years ago BORREL described minute bodies in the virus inclusions of fowl-pox which he considered to be the virus. In the following year VON PROWAZEK demonstrated similar structures—termed by him "elementary bodies"—occurring within and without the cells in vaccinial lesions, and in 1906 E. PASCHEN drew attention to the minute granules in variolous lymph and vaccinial material, commonly referred to now as "Paschen bodies." He found somewhat similar granules in varicella, and from a detailed study of these bodies, more particularly those present in the variolo-vaccine lesion, concluded that they were specific. Since that time many investigators have followed these pioneers in this field. The original observations of BORREL and PASCHEN have been confirmed and extended to other members of the group of filtrable viruses; but, despite this, the view that some, at any rate, of the filtrable viruses are minute coccus-like micro-organisms has not received general acceptance. There have been several reasons for this attitude. The technique required for the staining of elementary bodies is, relatively speaking, laborious and one which does not always furnish successful preparations even when carried out with great care. Added to this, artefacts, closely simulating elementary bodies, appear from time to time in such preparations to confuse the issue. But although these technical difficulties have probably delayed the recognition of the true nature of these elementary bodies, a much more effective brake on progress have been pronouncements by those speaking with authority. Evidence obtained from ultrafiltration experiments, which would not have been considered seriously were it not for the reputation of their authors, suggested that the disparity in size between virus and elementary body precluded any relationship. Expert microscopists have looked askance at these elementary bodies; in fact, at the discussion on filtrable viruses held by the Royal Society three years ago, Prof. J. G. G. LEDINGHAM alone upheld the possible ætiological significance of the Paschen body in vaccinia.

During the last two years, however, events have moved rapidly and the specific nature of some of these elementary bodies has been placed beyond all reasonable doubt. C. E. WOODRUFF and E. W. GOODPASTURE[1] have shown that a single Bollinger body—the inclusion body of fowl-pox—when isolated and washed free from any adhering virus is still capable of infecting, and that the contents of the Bollinger body consists of numerous elementary bodies (the Borrel bodies) embedded in a gelatinous matrix. And the ætiological significance of the Borrel bodies has been further advanced by LEDINGHAM who recorded in our columns last September that by fractional centrifugation he had succeeded in obtaining these bodies in relative purity and in demonstrating their specific agglutination with an anti-fowl-pox serum. Elementary bodies are present in psittacosis material, an observation first made independently in 1930 by W. LEVINTHAL, R. D. LILLIE, and A. C. COLES. These bodies stain easily and look like micro-organisms and on the strength of this and their more or less constant presence in virulent material LEVINTHAL[2] concluded that they were the causal organism and proposed the name *Microbacterium multiforme psittacosis*. His conclusion was not justified, but the additional evidence required to prove his thesis has now been supplied by S. P. BEDSON.[3] The latter has shown that the elementary bodies present in a suspension of virulent mouse-spleen can be freed from adventitious material by fractional certrifugation and washing and that the purified bodies which are capable of transmitting the disease are agglutinated specifically by an anti-psittacosis serum. In a like manner the original claim of PASCHEN, that the minute bodies described by him in vaccinia are the virus, has found confirmation. Applying similar methods to those employed by him in the case of fowl-pox virus, LEDINGHAM (loc. cit.) has shown that the Paschen bodies are specifically agglutinated by an antivaccinial serum. E. G. NAUCK and PASCHEN[4] have found that increase of virus in tissue culture is accompanied by a corresponding increase in elementary bodies, and finally, as they report on p. 823, Dr. G. H. EAGLES and Prof. LEDINGHAM succeeded in obtaining the Paschen bodies in a pure state by high-speed centrifugation and repeated washing and have shown that virulence resides entirely in the Paschen body.

Quite apart from the stride forward which these investigations mark in the study of filtrable viruses there is a point which calls for special comment, and that is that this progress has been achieved by the use of conventional methods alone. No sensible person would dream of decrying technical improvements and innovations. Refinements in dark-ground microscopy and the use of short wave-length light should prove of inestimable value in this field, especially in the case of viruses—and we know of several already—which are beyond the limits of microscopic visibility. But among the less-studied filtrable virus there must be some capable of investigation by the methods which have proved fruitful in the case of vaccinia and psittacosis, and the encouragement given by these successes should be of material help in the work lying ahead.

[1] Amer. Jour. Path., 1929, v., 1; 1930, vi., 713.

[2] Cong. Internat. Microbiol., Paris, 1930.
[3] Brit. Jour. Exp. Path., 1932, xiii., 65.
[4] Zeit. f. Bakt., 1932, cxxiv., 91.

LOW-SEGMENT CÆSAREAN SECTION.

SINCE WILLIAM SMELLIE, two centuries ago, wrote of the Cæsarean operation it "hath been performed both in this and the last century, and sometimes with such success that the mother has recovered and the child survives," we have advanced a long way. And yet a maternal mortality of almost 2 per cent. in so-called clean cases, which is the present experience of the country as a whole, can be viewed with little satisfaction. Its meaning will be better realised when we call to mind that the general maternal mortality-rate in England and Wales is about 4 per 1000. If every woman were delivered by classical Cæsarean section before the onset of labour or early in labour the death-rate would be 20 per 1000; Cæsarean section is, in fact, five times as dangerous for the mother as delivery by the natural passages. After labour has been in progress for a considerable time and sepsis has been introduced by internal examinations and repeated attempts at delivery the results of classical Cæsarean section are of course much more serious, and may in some cases be disastrous—a mortality of 25 per cent. or more being not infrequent. It was in the hope of remedying this state of matters that in 1907 the low-segment operation was introduced, in which the child is extracted through an incision in the cervix and lower segment of the uterus. The advantages claimed are briefly these. The spill of liquor amnii is limited to the pelvis so that there is less danger of general peritonitis if the fluid is infected; healing of the wound in the uterus is better, as the lower segment is at rest in the puerperium; he uterine wound is covered by the flap of peritoneum and seepage of lochia through the wound is thus prevented. For the same reasons the operation is held to be safer in infected cases. There is said to be less liability to post-operative adhesions as the uterine scar is situated low down in the utero-vesical pouch; shock is less and the convalescence is less disturbed as the intestines and omentum do not come into view during the operation. Finally, it is stated that rupture of the scar is less common in subsequent pregnancies and labours. On the other hand there can be no doubt that the operation is more difficult and may, unlike the classical, call for a considerable experience of abdominal surgery, while a longer time is required for extraction of the child. This increased difficulty is itself regarded by some as an advantage. There is probably no abdominal operation that is more frequently tackled by amateur surgeons than the classical Cæsarean, and there is reason to believe that this largely accounts for the high mortality.

The low-segment operation, with its various modifications, has gained steadily if slowly in favour, and sufficiently large series of cases have now been reported to justify an attempt to compare its results with those of the older operation. J. P. GREENHILL (Chicago) recently reported[1] 140 consecutive cases in which the low-segment operation was employed, with no maternal deaths and a fœtal mortality of 5 (3·6 per cent.). In three of these cases, the fœtus was dead before the operation was begun. The series included two eclamptics, seven cases of placenta prævia, and five of abruptio placentæ, while in 14 per cent. the membranes had been ruptured for 24 hours or more. He has also compiled statistics of 895 low-segment operations done by all operators including himself at the Chicago Lying-in Hospital, with a maternal mortality of 1·23 per cent. J. ST. G. WILSON (Liverpool) has related[2] a series of 50 cases with no maternal death and one stillbirth. V. COCQ compares[3] his results in 300 classical Cæsarean sections with those obtained in 50 low-segment operations. Of the former all but one were carried out on clean cases (dans les cas purs, he writes), the maternal death-rate being 2·3 per cent. Amongst the 50 low-segment operations there were 2 deaths (4 per cent.), but some of the patients had been in labour a long time, in some the membranes had been ruptured more than 24 hours, some had had several vaginal examinations before admission to hospital, and some had high temperatures before operation. Of the two fatal cases, one was exsanguine from unavoidable hæmorrhage before operation was begun; the other had acute pulmonary complications before operation and died of these some time afterwards. COCQ considers the low operation a much more formidable proceeding, and he deals in some detail with the difficulties encountered. In one case he found it necessary to do hysterectomy on account of downward tearing of the uterine incision. He concludes that the low operation is good in certain dystocias, but he adds a warning against undue enthusiasm. He would not, for example, substitute section for podalic version in every case of dystocia from contracted pelvis; it is, he thinks, still necessary to teach students, who may have to practise in the country, how to deliver by version in such cases. In clean cases he regards the classical as the better operation; it is simpler, and accidents in the course of the operation are rare. While after the low operation there may be less general infection there is more local sepsis in the pelvis and abdominal wall. When, however, infection is present he thinks the low operation is safer; its introduction has extended the indications for Cæsarean section. V. B. GREEN-ARMYTAGE speaks well[4] of the low-segment operation, which he has performed in 75 cases with 11 deaths (14·6 per cent.) and a fœtal mortality of 13·3 per cent.; 48 of his cases were "essentially septic" at the time of operation. "Before the war," he writes, "50 per cent. of the mothers who suffered the operation (classical Cæsarean with eventration of the uterus) after they had been hours in labour and were septic due to multiple examinations or trauma died of general peritonitis." Mrs. F. IVENS-KNOWLES has reported[5] 352 consecutive

[1] Surg., Gyn., Obst., October, 1931, p. 547.

[2] See THE LANCET, 1931, i., 977.
[3] Brux. Méd., March 20th, p. 579; March 27th, p. 595.
[4] Ind. Med. Gaz., 1931, lxvi., 184.
[5] Cæsarean Section, London, 1925.

classical operations with a maternal death-rate of 1·9 per cent.—a result to be regarded as extremely good when it is borne in mind that the series included all comers. In 24 cases premature labour had been induced instrumentally before operation (no mortality); in eight, forceps had been attempted (1 death); 14 were cases of eclampsia or other toxæmia (1 death); five were cases of accidental hæmorrhage (1 death); and there were 25 cases of placenta prævia (no death). H. R. SPENCER has reported [6] 120 cases, many of which were infected before operation, with four deaths. This should be compared with the 1·23 per cent. mortality at the Chicago Lying-in Hospital in 895 cases of the low-segment operation.

To sum up. While it may be granted that in infected cases the newer operation is attended with certain advantages that more than compensate for its greater difficulty, it is certain that if the patient is not in labour the difficulties are much increased. No doubt a true low-segment operation can be carried out at that period; only in 57 per cent. of GREENHILL'S series was the patient in labour before the operation was started. But the lower segment is then imperfectly formed; it is not thinned out as it is after labour has been in progress for some time, and it is in consequence more vascular. Further experience of the operation at this stage is necessary before its value can be finally assessed.

THE CINEMATOGRAPH IN MEDICINE.

THE cinematograph is as much a feature of modern civilisation as the motor-car and the aeroplane. For many years it has held a recognised place in general education, and instructional films of a high degree of excellence, portraying primitive peoples, features of animal and plant life, and the natural and architectural beauties of foreign countries appear to be an acceptable part of the programme in the usual places of entertainment. Films have proved valuable in disseminating information about modern agricultural methods, and the means of combating the various pests that attack crops and cattle. But the application of similar methods to medicine has been somewhat slow, and it is only within the last three years that the cinematograph has become a regular feature in scientific discussion and in the lecture theatres of medical schools. The reason is partly because medical education demands, perhaps more than any other, direct demonstration and personal guidance, partly because medical cinematography has not yet found its best methods.

The cinematograph has potentialities lacking in any other method of representation. It not only portrays form and motion, but through motion registers the dimensions and texture of the objects it records. It embalms the rarity; instances of rare diseases, or exceptional examples of more common ones, can be preserved for the study of successive classes. It bridges spaces of time, so that succeeding phases of some condition that may take months or years to develop may be shown in rapid sequence on the screen, allowing those who have only seen parts to visualise the whole, and all to form a coherent picture of what have been scattered glimpses. It provides an analysis of movements either too rapid or too slow to be appreciated by the eye. Accelerated photography, which shown at normal speed gives the slow motion film, permits the study of such subjects as normal and abnormal gaits, and the demonstration to students of the correct methods of tying ligatures and handling instruments. The division and growth of cells in tissue cultures, and the stimulating or retarding effect of drugs or radiation on this growth, may be recorded by retarded cinematography and projected at a speed that makes the process simple for the beginner, throws new light upon its phases for the expert, and, by its merely dramatic effect, emphasises the lesson for all. Again, outside considerations need not affect the sequence of a film, whose length and manner is chosen purely for its value as a teaching agent. Redundant parts can be cut out, and diagrams, explanations, or "close-ups" of essential apparatus, or part of the field of operation, may be inserted wherever further clarity is required, without the drawbacks that such acceleration or delay would involve in clinical work.

The whole question of the place of the cinematograph in medical education was reviewed by Prof. R. E. KELLY, of Liverpool, before the Surgical Section of the Royal Society of Medicine on April 6th. His lecture was illustrated by a series of films, which were all the more valuable in that they were taken by amateurs with a Cinekodak, and therefore showed what uses the teacher might make of the machine in his own work. The ground covered included operations upon the brain and spinal cord, upon an aneurysm of the carotid artery, and upon the breast with the diathermic cutting current, as well as records of the clinical features of the aneurysm before operation and the gait and facial movements of the cerebral tumour cases afterwards, and a demonstration of surgical emphysema involving the whole trunk. As Prof. KELLY explained, a film of an operation is not so much a record as an epitome, a series of excerpts showing the essential steps; but the skill with which his condensations had been made, and the high quality of his photography, should stimulate those of his hearers, whose efforts in the same field had proved disappointing, to try again. The majority of amateur surgical films are spoiled by poor focus. The method employed in Liverpool to obviate this fault—a measured piece of sterile silk fastened at one end to the wound and the other to the camera, which could then be moved to any angle at a fixed focus—is worthy of wider publicity.

The discussion which followed Prof. KELLY'S paper was concerned almost entirely with the use of the cinematograph in recording surgical operations, and speakers foreshadowed the employment of colour photography and sound recording for this purpose. Indeed it is in the field of operative surgery that motion photography has so far been

[6] Cæsarean Section, London, 1925.

chiefly exploited. For the expert and advanced student such films serve a definite purpose, for they allow the demonstration to a large audience of steps that can only be seen at operation by the surgeon and his assistants, and enable a lecturer to explain the details of a new operation and the use of some special instrument in the precincts of a medical society. But it is open to question whether a film of an actual operation, even when it is carried out by a leading exponent, is of any real value in the teaching of students. The absence of colour and contrast, the high lights that are reflected from moist tissues, the ooze of blood and movements of swabbing, and the multitude of unessential instruments that crowd the field on the screen, all lead to a confusion that can only be sorted out by the practised observer. A film of an operation is essentially an adjunct to a lecture by the operator himself, and the circulation of library films is very prone to degenerate from teaching to propaganda. The purely teaching film, designed and photographed for the instruction of beginners in the elements of operative surgery, is yet to be made, but a pointer of the way in which such a film should be arranged to be of the greatest value is provided by that dealing with infections of the hand, which is included in the Kodak library. Such a film might commence with a short history of the operation, and an account of the indications for its performance with diagrams of the main steps in the technique. The actual operation should be carried out on the cadaver, where the distance of the camera is dictated only by the size of the field to be shown and not by the needs of asepsis, for thus attention is not distracted and vision hampered by retractors, hæmostats, and the hands of assistants, while the tissues are not stained by blood, each step can be carried out deliberately, and the anatomical landmarks of the region can be pointed out as they are exposed. Each step should be explained by captions, and the special instruments that are required should be shown in "close-ups" before they are brought into use.

The cinematograph will surely find its place in all branches of the curriculum, and in the earlier years should fill an even more useful part than that which it has till now occupied in the later stages. It is hardly necessary to point out that the difficulty, insuperable in this country, of repeating before students more than a small number of the animal experiments upon which physiological knowledge is based, could thus be overcome; and that in anatomy films could be used to demonstrate, as no other method can, those structures which can only be shown in specially prepared subjects under exceptional circumstances. But the use of a cinematograph is not limited to photography. The animated cartoon, immortalised by "Felix" and "Micky Mouse," would delineate, with a lucidity that could not fail to carry conviction, the processes of intestinal rotation and all those intricate facts of embryology which even the pen of a KEITH has not been able to describe in words that the beginner can master without intent and repeated application.

THE USES AND ABUSES OF THE COLON.

FOR many years the colon has been a centre of interest to laymen and the medical profession alike. It has been douched, bathed, stimulated, soothed, anæsthetised, fed, and more recently psychoanalysed with an enthusiasm which, perhaps, no other single organ of the body can lay claim to have aroused. But in many quarters a note of warning and a plea for a more rational approach is now being sounded. Not only is the more elaborate nutrient enema now a thing of the past, but doubt has even been cast on the efficacy of the glucose enema as a means of administering carbohydrate. We have little positive evidence as to the actual amount of glucose which can be absorbed by this route, since neither the blood-sugar curves, nor changes in the respiratory quotient, nor even analyses of the subsequent fæcal return provide at all an accurate means of quantitative estimation. A recent study by Dr. F. L. SCOTT and Dr. J. F. B. ZWEIGHAFT,[1] carried out on medical students, showed a slight fall in the blood-sugar during the three hours succeeding the administration of 200 c.cm. of 10 per cent. dextrose solution per rectum, and this they suggest may possibly have been due to stimulation of pancreatic activity by the absorption of a small amount of dextrose, or more probably to chance variation; they also found that a variable and frequently considerable proportion of the dextrose administered may be recovered from the stools after two and one and a half hours.

Attention has also been drawn to the dangers both of unskilful administration and indiscriminate use of enemata and colonic lavage. Dr. H. H. RAYNER[2] has lately described the severe trauma and extensive sloughing that may result from the use of an unguarded bone or glass nozzle of an enema syringe—penetration of the anal mucosa being followed by fluid forced under pressure into the submucosa, while reference has been made in our columns (THE LANCET, 1931, i., 600) to the warning of J. FRIEDENWALD and M. FELDMAN[3] as to the inflammatory changes which may follow the repeated use of irritating chemicals, including sodium carbonate and even soap-sud enemata. A detailed summary of the technique, therapeutic applications, and dangers of colonic irrigations, written by Dr. W. H. BASTEDO for the American Council of Physical Therapy, appears, therefore, at an opportune moment.[4] While he distinguishes irrigations from enemata as having primarily the function of lavage whereas the latter are intended to produce defæcation, many of his observations are equally applicable to both. He considers the insertion of stiff tubing for more than 5 or 6 inches into the rectum not only useless, owing to the fact that greater lengths tend to curl up in the rectal ampulla, but dangerous. In colonic irrigation he recommends the use of an inlet and an outlet tube, and plain water at or just above body temperature; the irrigation should be

[1] Arch. Int. Med., February, 1932, p. 221.
[2] Brit. Med. Jour., March 5th, 1932, p. 419.
[3] Amer. Jour. Surg., 1931, xi., 23.
[4] Jour. Amer. Med. Assoc., Feb. 27th, 1932, p. 734.

given slowly, after the bowel has been emptied, to prevent the initiation of defæcation reflexes, the mid-level of the reservoir from which the irrigation is given being not more than two feet above the rectum. While the giving of an irrigation which shall "consume from 6 to 10 gallons and take nearly an hour" may seem to some a counsel of perfection for routine procedure in the hustle of modern hospital life, there will be little doubt that a more satisfactory lavage of bowel and removal of tenacious mucus will be obtained by this method than by the more hurried injection under greater pressure so frequently employed.

BASTEDO has a word of warning with regard to the over-zealous self-irrigator found so frequently among patients suffering from mucous colitis, and deprecates the exploitation of the procedure by nurses and others. Amongst the commoner mishaps he mentions bleeding from the rectum, the tearing of a rectal valve, and the injury or severance of a polypus. Properly employed, however, he considers that irrigation tends to improve rather than lessen the tone of the bowel wall and serves as a valuable therapeutic measure in washing out putrefactive material and loosening mucus above the defæcation area.

ANNOTATIONS

ATEBRIN IN MALARIA.

OF late years a new interest in malariotherapy has centred round the synthetic compounds produced by the I.G. Farbenindustrie in Elberfeld; for, as was predicted, plasmoquine has proved to be the prototype of other synthetic remedies. The latest of these, Atebrin, was first mentioned in THE LANCET by our Calcutta correspondent last week, and is the subject of a paper by Dr. Richard Green in our present issue. In the *Deutsche medizinische Wochenschrift* of April 1st, which contains a whole series of reports on this drug, Prof. Walter Kikuth gives the first account of its chemotherapeutic action. Formerly called erion, it is a yellow powder which melts at 245–255° C., and is soluble to the extent of 7 per cent. at 40° C. in neutral solution. From the chemical standpoint an alkylamino-acridin derivative, it was first synthesised by Mietsch and Mauss, and when tried in avian malaria (*Plasmodium præcox*), on the lines formerly employed by Roehl in his plasmoquine experiments, it was found to be less poisonous, but also less efficient in absolute figures. Atebrin showed itself 15 times weaker in the therapeutic sense than plasmoquine, and four times more powerful than quinine. In avian malaria it did not bring about any rapid sterilisation of the blood, as does plasmoquine, but behaved in this respect more like quinine; nor were more favourable results obtainable with such other strains of avian plasmodium as *P. elongatum* and *P. circumflexum*, forms which more closely resemble the subtertian parasite in man. By ingenious experiment on the hæmoproteus infection (*Hæmoproteus orizivoræ*) of the Java sparrow, Kikuth conclusively proved that the gametocytes which appear in the peripheral blood of this bird are eradicated by plasmoquine, whilst the schizont stages which develop in the endothelial cells of the lungs are attacked by atebrin, so that in individuals treated by this combined method relapses of hæmoproteus infection can no longer take place.

Prof. Franz Sioli writes upon atebrin in therapeutic malaria in general paralysis. His results are apparently very favourable, and entirely substantiate what has been learned from experimental avian infections. Atebrin can safely be given by oral administration in daily doses of 0·3 g. (3×0·1 g.) for a period of three days (total dosage 0·9 g.). Given in this manner it appears to cause the safe and permanent cure of experimental therapeutic malaria, being at least four times more reliable than plasmoquine. Apparently after three daily doses the patient remains parasite-free for at least 34 days. Under systematic and careful observation the intracorpuscular parasites begin to show marked morphological changes after 0·3 g., and after 0·6 g. they disappear entirely. Certain toxic effects are on record; thus 0·3 g. sometimes provokes intestinal pains, and in the great majority of cases the skin assumes a yellow tint. At first this was attributed to icterus, but the coloration has now been proved to be due to the natural pigmentation of the drug. Daily analysis of the urine showed no marked excretion of urobilin or bilirubin as the result of absorption of atebrin, and this suggests that it has no toxic effect on the liver. F. M. Peter, who has used the drug in Gurbanesti (Rumania) in cases of natural infection by malaria, is able to show that in this compound we have a schizont-destroying agent of the first order. The material consisted of three cases of benign tertian malaria, the total dose of atebrin being 1·0 g. The effect on the temperature curve, as well as upon the parasites, was striking. The smaller ring forms (or schizonts) were first attacked, and the gametocytes later, while the shrinkage of the spleen was rapid and complete. In two cases of natural subtertian infection somewhat similar results were obtained; the schizonts disappeared after 24 hours, but no effect upon the gametocytes (crescents) was ascertainable. P. Mühlens has had the advantage of much more clinical material in the Hospital for Tropical Diseases in Hamburg. From his report[1] it appears that from Nov. 24th, 1930, to the end of February, 1932, 122 cases (17 tertian, 8 quartan, 85 subtertian, 2 cases of quinine idiosyncrasy, and 10 of malarial complications) have been treated alone with atebrin, or with atebrin combined with plasmoquine. The results were similar to those already related. In subtertian infections the effects upon the schizonts were far more remarkable than those of quinine or plasmoquine. Using a combination of atebrin (0·3 g. daily) with plasmoquine (0·03 g.) the gametocytes disappeared in three to six days. Mühlens further satisfied himself that the action upon quartan malaria was equally satisfactory. He has been able to employ a total dosage of 4·8 g. without producing any toxic symptoms, and considers the yellow colour of the skin to be due to acridin-staining which sometimes persists for two to three weeks. In his opinion, atebrin is equally satisfactory in all three forms of malaria, but in combination with plasmoquine it attains its maximum efficiency in subtertian infections. However, in heavy ring infections he thinks that for the first two days intramuscular quinine should always be exhibited, to be reinforced later by atebrin and plasmoquine. It is good to

[1] Münch. med. Woch., April 1st, p. 537.

note that atebrin is well borne in cases of quinine idiosyncrasy and in the pre-blackwater state. In Mühlens's opinion the atebrin treatment of malaria is in its ultimate results at least equal to those obtained with chinoplasmin and plasmoquine compound.

We therefore welcome this the latest addition to malarial therapeutics. The early promise of this branch of chemotherapy has already borne good fruit, and we have now been given two new and powerful remedies. But in order to estimate the exact value of atebrin in the campaign against malaria a vast amount of work will have to be done.

GRADE A HEALTH FACTS.

In a recent lecture delivered at the Royal Institute of Public Health [1] Prof. H. R. Kenwood remarked on the economy of effort and money which would result if all health propaganda could be made sound and therefore harmonious. Uniform health advice would, he said, have great weight with the public. The same thought is moving in America, as seen in the sound and vigorous attitude towards health education taken [2] by Dr. Donald B. Armstrong, a high official in one of the largest American life assurance companies. Dr. Armstrong disagrees emphatically with what he calls the "extreme individualism and pessimism" shown by Dr. Robert Hutchison at the Winnipeg meeting last summer. He is certain that health must be taught to the public, and he agrees substantially with the manner of teaching set out in a leading article [3] on Dr. Hutchison's address. Dr. Armstrong demands the presentation of health rather than disease, and of health as a basis for growth, character, and happiness. He classifies facts into three grades: scientifically certified facts; items that are probable but are not quite certain, including certainties of a previous generation which are now becoming questioned and possibilities that increasing experience is making more probable; and items extensively used as facts, especially for commercial exploitation, which are either erroneous or designedly misleading. He classes the work of Dr. Sherman and others on the vitamins as Grade A facts suitable for public examination, and he feels on fairly sure ground when teaching the value of sunlight and the dangers of communicable disease. Nevertheless, he admits difficulties in method. While to a certain extent he approves as a sound objective the slogan "Find Disease Early," he points out that the periodic health examination, though good in theory, is a very frail instrument in practice. The public is not yet educated, he says, to go to the doctor early enough; the doctor is not sufficiently interested nor able to carry out all the necessary tests, and few communities can direct the public to proper sources of such service. He holds, however, that the public should be taught not to be afraid of fact, and that health suggestion comes better from the physician on a basis of fact than through quackery and patent medicine advertisements. One of the chief needs of the community is, he thinks, a mechanism for individual guidance, and this, he suggests, could best be given by the private physician under the auspices of county medical societies. He warns medical publicists to be more cautious in their popularised forecasts. The slogans "No Tuberculosis by 1915" and "No Diphtheria by 1930" aroused great interest and effort and the fact that they were not realised caused little disappointment, but he thinks it inadvisable to prod the frail public memory too frequently with explosive health campaigns, the promise of which can hardly ever be fulfilled. While granting the necessity to be assertive and dogmatic, he adds, "There is some admitted hokum in our health educational program, and the public is in a debunking mood. Let us therefore keep, so far as possible, within the realm of the attainable." Yet he tolerates health rules such as those advising the consumption of a certain number of glasses of water a day or the enjoyment of an average of eight hours' sleep every night, the value of exercise in promoting longevity, and the necessity for brushing the teeth twice a day—justifying them by the need for being direct, simple, and dogmatic.

In the same issue of the *American Journal of Public Health*, Mr. George F. Wright, Editor of the *Montreal Star*, tells us what constitutes health news from the point of view of the lay press. He points to a fault, to which some of us may have to plead guilty—viz., a rooted objection to the presentation of medical research and discovery in an attractive form. Nobody, he says, would read an account of a discovery presented in a methodical and orderly fashion, for it would be immeasurably dull. Nevertheless, he asserts that a strict adherence to fact is the one motto which an editor is always placing before his staff. He believes that the cause of public health is best advanced by the newspaper reader getting into his brain the necessity of carrying out certain simple rules of living. For this the constant reiteration of plain truth is of some value, but the artful presentation of that truth in many varying forms counts for much more.

[1] Jour. State Med., March, 1932, p. 125.
[2] Amer. Jour. Pub. Health, March, 1932, p. 271.
[3] THE LANCET, 1931, i., 357.

A PARASYMPATHETIC CENTRE IN THE HYPOTHALAMUS.

The influence exerted on metabolism and visceral activity by the two opposing divisions of the autonomic nervous system—the sympathetic and parasympathetic mechanisms—has long been recognised. The precise situation of the centres controlling these mechanisms, however, is only just coming to light. A considerable amount of indirect evidence has pointed to the hypothalamic grey matter in the floor of the third ventricle as the seat of the sympathetic nucleus, and direct proof has recently been forthcoming, in the demonstration by J. Beattie, G. R. Brow, and C. N. H. Long,[1] of Montreal, of a tract of fibres linking up this region of the brain with the lateral horns of the grey matter of the spinal cord. About the position of the parasympathetic centre there remains some doubt. Harvey Cushing [2] believes it to be situated, like the sympathetic nucleus, in the hypothalamus, and has shown that injection of pituitrin into the ventricles of the brain of human subjects leads to increased salivation and to increased mobility and hypersecretion of the stomach. J. Beattie [3] has just reported, in outline, some experiments on animals which support Cushing's suggestion. Beattie stimulated the anterior portion of the hypothalamus electrically and studied the effect on the stomach, in some instances by direct examination of the exposed organ, in others by suturing electrodes into the stomach wall and obtaining graphic records on electrocardiographic plates. He found that hypothalamic stimulation causes increased peristalsis

[1] Proc. Roy. Soc., B, 1930, cvi., 253.
[2] Proc. Nat. Acad. Sci., 1931, xvii., 163, 239.
[3] Canad. Med. Assoc. Jour., March, 1932, p. 278.

and a flow of secretion containing hydrochloric acid and pepsin, changes which could be prevented by previous section of the vagi. When the vagus was divided and its central end anastomosed with the peripheral end of the cut phrenic (a sufficient interval being allowed for regeneration), hypothalamic stimulation caused contraction of the diaphragm. Another significant observation was that prolonged stimulation led to the appearance of small areas of hyperæmic mucosa near the lesser curvature of the stomach. Beattie's preliminary results therefore not only afford evidence of the situation of the parasympathetic centre, but also promise to throw some light on the ætiology of gastric ulceration.

THE MEGALOCYTIC ANÆMIAS.

THE old classification of anæmias as primary or secondary has rapidly given way in the last few years to one dependent upon the size of the red cells. C. Price-Jones has recently elaborated his earlier work on red cell size and has determined by refined statistical methods both the smallest and largest possible normal red cell distribution curves. A condition, therefore, in which the red cells show on measurement a curve falling to the right of the largest possible normal can be described as a megalocytic anæmia and one where the curve falls to the left of the smallest calculated normal, as a microcytic anæmia. Certain cases within normal limits have been described by M. M. Wintrobe as normocytic. This variation in size of the red cells appears to have a direct relationship to the ætiology of the anæmia. Thus the microcytic anæmias respond to massive iron dosage, while the majority of the megalocytic anæmias can be relieved by adequate administration of liver extract or its substitutes. The problem of the megalocytic anæmias is becoming increasingly complex however, as was shown in the discussion at the Royal Society of Medicine reported on p. 836. Castle's fundamental observations on the ætiological significance of a failure of gastric secretion in Addisonian anæmia forms the basis for his hypothesis that a similar failure is the cause of all megalocytic anæmias, associated in some instances with faulty absorption. This is supported by the finding that the majority of such anæmias are associated with a demonstrable gastric lesion: sprue, idiopathic steatorrhœa (which probably includes the majority of conditions described as fatty diarrhœa, cœliac disease, chylous diarrhœa and pancreatogenous diarrhœa), gastro-colic fistula, intestinal anastomoses and resection, gastrectomy, carcinoma of the stomach, and bothriocephalus anæmia. The group are all relieved by the suitable administration of the effective principle in liver. It is possible that the tropical anæmia described by Dr. Lucy Wills in which there is no demonstrable gastric deficiency is dependent upon lack, not as in the others of Castle's intrinsic factor, secreted in the gastric juice, but of his extrinsic factor supplied in the food, since all Indian diets are notably deficient. Such a case of typical Addisonian pernicious anæmia occurring in a strict vegetarian with apparently normal gastric secretion and relieved by diet alone has been described.[1] Dr. Goodhart discussed, however, an extremely interesting group of cases associated with a variety of conditions as pulmonary tuberculosis and Hodgkin's disease which failed to react to liver or liver extract given by mouth and which in some cases showed no obvious intestinal lesion. They had certain features in common which distinguished them from Addisonian pernicious anæmia. The Price-Jones curve appeared on inspection to be relatively symmetrical and though, as Dr. Price-Jones remarked, this does not mean that it was so mathematically, it was an appearance common to the group and therefore perhaps significant. Many of them, in spite of a leucopenia, showed a shift of the Arneth count to the left which is never seen in the idiopathic form and in none were the characteristic multilobed polymorphs found. Dr. Vaughan and Dr. Hunter also point out in their observations on idiopathic steatorrhœa published in our present issue that Addisonian pernicious anæmia can be clearly differentiated from a further large group of megalocytic anæmias possessing certain features in common. Sprue, tropical anæmia, megalocytic anæmia associated with gastro-colic fistula, and idiopathic steatorrhœa have a low indirect van den Bergh reaction, as did many of Dr. Goodhart's cases, suggesting that there is less disturbance of pigment metabolism than in the idiopathic type. Poikilocytosis is not a marked feature of the stained films and hydrochloric acid is frequently present in the gastric juice or returns after treatment. The anæmia of sprue, tropical anæmia, and idiopathic steatorrhœa responds as dramatically to marmite as to liver extract while Addisonian anæmia is unaffected by marmite. Marmite is a complex substance and it is not yet clear how far its action is associated with its vitamin B content. It is important that in the future all megalocytic anæmias, other than the idiopathic type, should receive adequate treatment with marmite, which is relatively inexpensive, in order to determine how far a response to the effective principle in liver is peculiar to Addisonian pernicious anæmia. Information on this point should help towards a reasonable classification and understanding of the pathology of megalocytic anæmias.

[1] Kern, R. A.: Ann. Int. Med., 1931, v., 729.

DESENSITISATION OF RHEUMATIC CHILDREN.

MANY supporters have been found for the theory that the clinical manifestations of "rheumatic fever" represent the allergic response of a subject sensitised, by previous infection, to certain strains of hæmolytic streptococci. Though by no means proven, this theory explains the facts better than any other yet put forward, and may be regarded as a base from which to attack this condition, which has hitherto been approached along purely empirical lines. It is during the recurrences that the worst damage is done, and it was first pointed out by Swift and his collaborators[1] at the hospital of the Rockefeller Institute that, granted the allergic view of the condition to be correct, the rational thing to do would be to try to desensitise the subject after the first attack, in the hope of thereby reducing the incidence and severity of later illness. The possibilities of this procedure have lately been explored by Wilson and Swift,[2] working in the Cornell University Medical School, and the results have been encouraging. They took a group of about 180 children who had suffered from rheumatic fever, and divided them into a test and a control group. The children of the test group received intravenous injections of a vaccine made up from hæmolytic streptococci isolated from a rheumatic subject; the

[1] Swift, Homer F., Hitchcock, C. H., Derick, C. L., and McEwen, C.: Trans. Assoc. Amer. Phys., 1930, p. 45.
[2] Wilson, May G., and Swift, Homer F.: Studies from the Rockefeller Inst. Med. Res., Reprints, 80, 1932 (from Amer. Jour. Dis. Child., 1931, xlii., 42).

injections were given intravenously, beginning with a dose of 250,000 and working up to 10,000,000; the inoculation was done during two successive years: in the first throughout the late summer, autumn, winter, and early spring; and in the second in winter and early spring only. A comparison of the case-histories of the two groups shows a significant diminution both in the incidence and severity of rheumatic manifestations in the treated group. The investigation is of interest from several standpoints. Apart from its value as an indication of a method of attack upon one of the most disabling of all diseases, it draws attention afresh to the allergic factor, consideration of which has been almost swamped of late by concentration upon "infection." Further, it emphasises a side of vaccine therapy which has been comparatively neglected. Asked what they expect to do with a vaccine, most medical men would probably assert that they hope to "immunise" the patient. Certainly the possible uses of desensitisation are too often overlooked.

HOUSING IN KENSINGTON.

FEW boroughs have such an abrupt division of amenities as Kensington, where the southern half is a superior residential quarter and the northern an area of overcrowded tenements. The recent survey of housing in Kensington made by Irene T. Barclay and Evelyn E. Perry quotes repeated examples of the following kind:

"Two basement rooms, the back one damp and dark. The family here is a husband and wife, a boy of 13 and girls of 11, 10, 8, 5, 3, and 1—nine persons. The tenant has regular work and an average wage of £3 5*s*. per week. He wants open air and a garden and is anxious to go to an outlying L.C.C. estate if he can have a cottage at a rent within his means. . . "

In a foreword to the survey by Mrs. Victoria de Bunsen and Major-General Neill Malcolm the problem is described as overcrowding aggravated by bad basements. At the 1921 Census the Registrar-General found that the number of persons living at a room-density of more than two per room was no less than 26,456, and the surveyors conclude that the whole building, carried out by combined public and private activity since the war, has only served to prevent overcrowding from becoming worse. Legal overcrowding, based on air space per person, is not the rule, but the inadequacy of the standard adopted can be appreciated from the fact that it is possible for a parent and eight children to live in two rooms of an ordinary Kensington house without being legally overcrowded; but on the Registrar-General's standard overcrowding is present in 76 per cent. of cases. It is, apparently, seldom possible for a husband and wife to occupy the same bedroom without involving the family in a breach of the by-laws relating to separation of the sexes; and a living room not used also as a bedroom is a rarity. The chief obstacles to any building programme sufficiently large to relieve the situation are, of course, the scarcity of sites and lack of funds. The financial requirements could be covered by quite a small addition to the rates; a building scheme recently approved by the borough council would mean an addition of only twopence a year to a house rated at £100. The scarcity of available sites does not seem to be insuperable, and the surveyors think it would be possible to effect a very great improvement within a few years. Many of the existing buildings in a street named in the report are insanitary and verminous and have been condemned. The report of the school doctor shows that children coming from this street are subnormal in health, and compare unfavourably with those from other streets, but while there is no alternative accommodation for the 58 families inhabiting the street it cannot be pulled down. In the words of Dr. Leonard Huxley, writing recently in the Cornhill Magazine, "why not avert the blow instead of healing the wound? We tend the sickly but do not create the healthy—we punish wrongdoers but see the good seed swamped in the morass—we educate, but there is no chance of knowledge spreading in such hopeless surroundings."

The Kensington Housing Association is holding an open meeting at the Kensington Town Hall on Monday, April 18th, at 8.15 P.M., at which Dr. Raymond Unwin will speak on the town planning of Kensington.

COMPULSORY STUDY OF THE HISTORY OF MEDICINE.

Prof. W. Szumowski of Cracovia, Poland, recently read a paper at the Eighth International Congress of the History of Medicine advocating the compulsory teaching of the history of medicine in the universities of the world. Such teaching, he thinks, should be given to the medical student during the first year of his training and should be rendered effective by an examination. The suggestion, no doubt, is good in theory but is impracticable in practice, at any rate in Great Britain. The difficulties of educational authorities in dealing with the medical curriculum are acute, and the introduction of another compulsory subject would not be contemplated by any university or corporation. A few students having a bent towards the historic or antiquarian side of their studies will always show an interest in the history of medicine, but its teaching should be post-graduate and its study left to a more mature age, when leisure, curiosity, and a cultivated taste have developed an appetite for literary knowledge; and by this time formal instruction becomes unnecessary, while compulsory study has never produced satisfactory results in England when voluntary efforts have often been fruitful. The Section of History of the Royal Society of Medicine provides a meeting-place where historical comment and the outcome of historical research can be ventilated, while students' clubs, formed in connexion with their own hospitals or elsewhere, give opportunity for similar discussions among the younger generation.

Summer Time will commence in Great Britain, Ireland, the Channel Islands, and the Isle of Man on Sunday morning next, April 17th, at 2 A.M., when the hands of timepieces should be advanced one hour. It will end on Sunday, Oct. 2nd.

SCARCITY OF HOSPITAL MAIDS.—The matron of the Enfield and Edmonton Joint Hospital reports a difficulty in obtaining maids, most of whom are quickly incapacitated by illness, the result of the "desperately hard" work. Lack of accommodation makes it impossible to employ a larger number of girls. The difficulty is to be met by employing married women when needed—single women will not apply for daily work—and by giving three weeks' annual holiday instead of a fortnight. It was stated that other hospitals are experiencing a similar difficulty.

PANEL AND CONTRACT PRACTICE

Distribution of the Central Pool.

THE central pool, it may be recalled, is the sum of money represented by the number of insured persons in the country multiplied by the capitation fee. The number of insured persons must in the nature of things be always varying owing to deaths, new entrants into insurance, members becoming disentitled to benefit, and so forth. The figure has therefore to be arrived at by actuarial calculation by the Government Actuary. The method employed has been tested on behalf of the profession by an independent actuary and has been proved to be a sound method of calculation. As a further safeguard it has been usual for the Distribution Committee (on which are representatives of the Government Actuary, of the Ministry of Health, of the Insurance Acts Committee, and of rural practitioners) to meet annually to advise the Minister of Health as to the method of distributing the central pool amongst the various insurance committees.

The Distribution Committee did not meet formally this year, but figures have been compiled at the Ministry of Health from returns given by insurance committees and others show that for 1931 the calculation of mileage grants to rural areas have been based on recently obtained figures of claims instead of as last year on those for 1927. Scrutiny of these figures shows that 14 counties (Bedfordshire, Cornwall, Durham, Essex, Herts, Isle of Ely, Kent, Lancs, Rutland, Sussex East, Sussex West, Worcestershire, Yorks North, Westmorland) have on each occasion increased their mileage claims, whilst 11 counties (Bucks, Cambs, Isle of Wight, Lincoln Lindsey, Oxford, Wilts, Hereford, Leicestershire, Notts, Salop, Bury) have on each occasion lost a proportion of that grant. Figures of other committees have not altered much one way or the other. In 1930 the Distribution Committee advised that units should be calculated from the doctor of choice and not from the nearest available doctor. Insurance committee returns had previously varied on this point.

1 unit is	obtained for	2 miles and under 3	from
2 units are	each insured	3 „ „ „ 4	his
3 „ „	person living over	4 „ „ „ 5	doctor.

The total mileage grant is £250,000, divided proportionately amongst the insurance committees according to the number of units claimed. There is an additional allowance for specially difficult places.

The apportionment of the central practitioners' fund for the year is arrived at by adjusting the index register apportionment of each insurance committee. The figures supplied by the Ministry are expressed as a percentage of the whole insured population—e.g., London has 12·9748 per cent. of the insured population, and therefore of the fund. The first adjustment of this is for temporary residents. Some committees, e.g., those in seaside resorts, have a percentage addition. Others, e.g., London, have a deduction made for temporary residents, more of whom they send away to other committees than they receive from them. The deduction for London for 1931 was 0·0714 per cent. Deductions are also made for institutions recognised under the Insurance Acts, for mercantile marines, and for persons who are allowed to make their own arrangements. London has no institution deduction, but it loses 0·0356 per cent. for mercantile marines, and 0·0091 per cent. for "own arrangers." In this way a net figure is arrived at for each committee, the London net figure becoming 12·8587 per cent. These net figures added together do not make 100; a final adjustment is therefore made so that they do become percentage figures, and this adjustment makes London's final figure 13·0425 per cent.

These figures illustrate how the character of insurance practice varies in different localities, and how insurance committees vary in their decisions upon "own arrangers." The Ministry of Health also supplies the Distribution Committee with the quarterly count during the year of each insurance committee index register. These figures show the movements of the insured population from one area to another, and where the population is going out of insurance. In the county boroughs the tendency is as follows:—

Count going up—plus.	Count going down—minus.	
Brighton.	Barrow.	Bradford.
Blackpool.	Birkenhead.	Burnley.
Hastings.	Bristol.	Halifax.
Southend-on-Sea.	Newcastle.	Huddersfield.
Southport.	East Ham.	Middlesboro.
Birmingham.	West Ham.	Oldham.
Manchester.	West Hartlepool.	Nottingham.
Croydon.	Bolton.	Preston.
Oxford.	Bootle.	
Worcester.		
Exeter.		
Portsmouth.		

The last set of figures supplied to the Distribution Committee shows the amount paid per name on doctors' lists for each committee. The figures this year relate to 1930, and so do not take into account the 10 per cent. deduction. Committees with a payment of less than 9*s*. evidently have more names on their index than should be there; presumably duplication is going on and the necessity arises for the "clearance" of the register. The same thing may be caused by the allocation to doctors in the area of all names who have not chosen a doctor; this, however, is not a common practice amongst insurance committees. Those committees whose payment per capita is over 9*s*. are frequently those whose locality makes them likely to receive many temporary residents. The figure for London is 9*s* 1*d*.; for Blackpool, 10*s*. 2*d*.

The total number of insured persons for last year on the central register was 14,896,630, being the mean of four quarters' counts. The total fund available for the central pool would have been £6,638,051, but with 10 per cent. deduction in respect of the four quarters the amount available for the year was £6,467,625. With 10 per cent. deduction for the whole year the fund is estimated at £5,800,000.

References to Regional Medical Officers.

"Both personal experience and an accumulating mass of correspondence in the medical press," writes Rural Panel, "bear witness to a widespread and growing discontent with the present system by which the selection of patients to be referred to the regional medical officer is governed. When the panel practitioner finds that he is requested to provide information about patients who have left the district weeks before, who are moribund, who are 'referred' after three days of an illness such as 'acute tonsillitis,' or who have been 'referred' so repeatedly that they 'sign off' in disgust though incapable of resuming work, he not unnaturally blames the person who is ostensibly responsible for the selection—i.e., the regional medical officer.

"It now has been made clear, however, that the choice of whom to 'refer' is not in any way under the control of the R.M.O., but rests entirely in the hands of the approved society concerned. Moreover, the practice of different societies varies enormously. In an investigation by the Reading Panel Committee it was found that 70 per cent. of the 'references' came from three industrial societies, while less than 1 per cent. were 'referred' by friendly societies. In one case a doctor wished to refer a patient to the R.M.O. with a view to getting further advice on his condition, and was told that the society in question had never 'referred' one of their members yet, and didn't intend to do so! Again, one society is alleged to refer patients without any consultation with their local officers at all. It is also alleged, incredible as it may seem, that Form R.M. 2 may be sent out by the society to the panel practitioner direct, in spite of the fact that it is addressed from and signed by the R.M.O. This is supported by the fact that the interval between the issue of the first certificate and the 'reference' is sometimes too short—e.g., two days—for it to have been through the hands of the R.M.O.

"All this does not mean, presumably, that the system has been changed, but that since the trouble about 'excessive certification' arose, and since the publication of the now notorious I.C. 329 references to the R.M.O. have increased to such an extent that the panel practitioner, instead of regarding them as a rather bad joke, feels like a babe in the wood being buried alive by showers of R.M. twos and threes. He is therefore beginning to inquire as to what particular robin is responsible for this embarrassing fate. The results of these inquiries, if correct, are certainly surprising, and throw a new light on the position and functions of the regional medical officers. These gentlemen, it appears, instead of being the principal villians of the piece recede into the status of hired bravoes, a position which they doubtless feel as acutely as anybody.

"Seriously, however, the conclusion cannot fail to be drawn that a very great deal of time and some money is being wasted, and it seems an opportune moment for an inquiry by the Ministry into the whole system."

National Formulary.

The London Panel Committee at its last meeting returned to a consideration of the directions for use printed with the formulæ in the National Formulary. A motion submitted by the pharmacy subcommittee, "that the Insurance Acts Committee be informed that the Panel Committee is of opinion that instructions to pharmacists for the administration of mixtures should be deleted from the next issue of the National Formulary," was lost. It was felt that the convenience of many panel prescribers should not give way to the difficulties of the few who have trouble with the directions.

Thermogene Wool.

The same subcommittee reported that the London Insurance Committee, under Article 4 (1) of the Medical Benefit Amended Regulations, 1930, has referred to the panel committee for consideration an appeal against its decision that the substance ordered (thermogene wool) did not form part of medical benefit; in other words, that this was an appliance and not a drug. The appeal was heard by the subcommittee, representatives of the insurance committee and of the Ministry of Health being present. The appeal was allowed on the ground that the action of the capsicum content of the wool was the chief reason for ordering this substance, and the action of capsicum was undoubtedly that of a drug. A court of referees may be set up to make the final decision.

Interpretation of "Personal Service."

The ethical subcommittee of the London Panel Committee has considered the case of the elderly practitioner and his assistant mentioned in these notes some weeks ago.[1] This case, in accordance with regulations, was referred to the panel committee by the insurance committee after the latter had passed a resolution that permission to employ an assistant should be withdrawn. The panel committee, after pointing out that there had been no complaint by any insured person and that the regulations on personal service—namely, continuity of treatment and availability of principal if asked for—had been carried out, passed the following resolution:—

That the committee do inform the insurance committee that although it strongly objects to the principle of "farming out," after investigation it is of the opinion that the conduct of this practice does not come within that category. It considers that the insured persons concerned have not suffered in any way by reason of the manner in which the practice is being conducted.

The committee recognises that whilst the principal practitioner does not take a very active part in the conduct of the practice, acting chiefly in a supervisory capacity, he is undoubtedly available for consultation and supervision, and the results of this arrangement are in no way detrimental to the interests of the insured persons concerned, the principles of continuity of treatment and availability on request having been preserved. The committee is further of opinion that it would be unreasonable to withhold permission to employ an assistant in this case, and would point out that such action would be injurious to the practice, as it would entail a fresh practitioner being brought in, the present assistant being unwilling to accept a partnership.

The matter will now presumably go to the Ministry for final decision.

[1] THE LANCET, Feb. 27th, p. 478.

BRITISH EMPIRE CANCER CAMPAIGN.—In the absence of Lord Reading, Sir John Bland-Sutton presided at the quarterly meeting of the Grand Council of the British Empire Cancer Campaign held in London on April 11th. The following grants, totalling £10,000, were made in furtherance of cancer research: £500 to St. Mark's Hospital, £2500 to St. Bartholomew's Hospital, £1500 to the Cancer Hospital, and £5500 to the Middlesex Hospital. The nomination of Mr. W. Sampson Handley to act as the representative of the Queensland Cancer Trust on the Grand Council, and the election of Dr. G. Fildes, as an additional member of the Radiology Committee, which acts jointly for the Medical Research Council and the Campaign, were confirmed. The report of the judges of the 1931 Garton prize essays on the Early Diagnosis of Cancer was received. The judges reported that in their opinion none of the essays was worthy of the prize and the Council accordingly resolved that the prize for 1931 be not awarded. Dissertations for the next Garton prize, on the Biological Effects and Mode of Action of Radiations upon Malignant and other Cells, are due to be received not later than Dec. 31st, 1933. Arrangements have been made in collaboration with the Queen's Institute of District Nursing and the public health section of the College of Nursing, whereby copies of the Campaign's official publication "The Truth about Cancer" will be made available for the active members of those organisations.

HOSPITAL SWEEPSTAKES AND PUBLIC ASSISTANCE.—In consequence of the Louth County Infirmary having received £30,000 from the Free State Hospital Sweepstakes the Louth county council has refused to continue its annual subscription of £1400. The council contends that the infirmary now has plenty of money, and is likely to receive more from the recent sweepstake on the Grand National. The infirmary's reply is that it is no better off than before, since the new invested money merely replaces the public grant. The county council's rejoinder is that for many years it has paid £700 in excess of its legal liability because of the infirmary's urgent need of money, and that it ought to be credited with the excess now that the hospital is no longer financially embarrassed. The infirmary claims that under an Act of Parliament it is entitled to a minimum sum of £320 per annum.

SPECIAL ARTICLES

THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE.

THE Court of Governors of the London School of Hygiene and Tropical Medicine has elected Sir Austen Chamberlain as chairman of the Governors and after the ceremony, which took place on Thursday, April 7th, Sir Austen presided at a luncheon given in the library of the School.

Sir Hilton Young proposed the health of Sir Austen, and pointed out his peculiar fitness to fill the post, and meet the responsibilities thus assumed. His appointment, said Sir Hilton, was the outward and visible sign of the association of his family with the development of tropical medicine. He recalled the original work of their chairman's father, Joseph Chamberlain, and the activities of his brother, Mr. Neville Chamberlain, who, when Minister of Health, laid the foundation-stone of the premises in which they were sitting. Speaking himself as Minister of Health, Sir Hilton said that the fundamental benefits which the Empire could bestow upon its dependencies were two, peace and health. The provision of medical and hygienic services in the colonies promoted these two objects, but the services could only be carried on by the setting up and maintenance of active scientific research.

Library of the London School of Hygiene.

Sir Austen, in replying, was reminded that 40 years ago his father, at the inaugural meeting of the School, had pointed out that the greatest enemy of the Empire in its dependencies was not the survivals of barbarous customs, nor the hostility of opposing chiefs, nor the geographical and natural attributes of countries where nature had held unfettered sway; it was the incidence of disease which destroyed or weakened the personnel of those engaged in the labours of colonisation, killing many and weakening or shortening the lives of very many more. He read the following extract from the *Lagos Standard* of September, 1898:—

"There is no doubt that something should be done to relieve the grave-diggers from the strain of the work to which they are continually subjected. The demands of a constantly increasing death-rate, which has caused the cemeteries to be enlarged, make it necessary that the number of grave-diggers should be increased. No holidays—at it from 6 A.M. to 6 P.M. every day, Sundays included, for the grim Reaper is ever busy."

"While I do not," he said, "recommend Lagos as a health resort the picture in 1898 enables us to understand the gulf which had been traversed during 40 years. The huge improvement in the death-rates of various tropical dependencies can only stimulate further work, and how vast that work is would be obvious when the long list was recollected of diseases which still infested these countries." It was true, he said, that many of the old problems were no longer insoluble, and that we could look forward to the eradication or the rendering innocuous of pestilences which once were a scourge; but in tropical disease there was urgent work yet to be done, both humanitarian and utilitarian. And as the diseases were conquered the development of trade would follow. He next referred to the need of turning attention to the problems of health at home, for it would be wrong, he said, even on this occasion, to look only at tropical medicine. On all sides there was a field of inquiry and research which grew larger with every discovery, while every discovery in one department of medical science helped not some particular area or some particular country but the world at large. He knew that the School would receive the coöperation of other countries in endeavours made for the general service of mankind. Sir Austen concluded by proposing the toast of Sir Holburt Waring, the retiring chairman of the Court who had for eight years assisted in the developments of the institution.

Sir Holburt Waring briefly replied.

A large and representative gathering of guests was present and among the telegrams of regret for inability to be present was one from Sir Henry Wellcome, sent from New York, which ran as follows: "Cordial greetings and best wishes for the continued success of the noble work founded and organised by Joseph Chamberlain and Patrick Manson. Deeply regret absence."

CORRESPONDENCE

THE GALL-BLADDER AND CARDIAC PAIN.

To the Editor of THE LANCET.

SIR,—I am delighted to find that Dr. C. H. Miller is calling attention to the association of cardiac pain with disease of the gall-bladder. The connexion is not yet generally appreciated. I propose in the near future to deal fully with my experience of the relation of gall-bladder infections to troublesome cardiac disease. It has been my lot on many occasions to find that "heart disease" has been the reason given for refusal of the benefits of surgical treatment to patients suffering from cholelithiasis. In such cases it is a common experience to find that removal of the gall-bladder is followed by a restitution of the heart to a normal condition, or by a very considerable measure of relief to cardiac symptoms. Sir James Mackenzie was first responsible for my interest in this subject, by asking me to operate upon a number of his "cardiac" patients. I removed the gall-bladder and the "heart disease" not seldom disappeared. Disease of the myocardium may often be regarded as the strongest indication for surgical measures. The relationship between infections of the gall-bladder and cardiovascular disease has hardly received the attention it deserves since Sir James Mackenzie and Sir Humphry Rolleston so clearly described it.

I am, Sir, yours faithfully,

Portland-place, W., April 11th, 1932. MOYNIHAN.

ADSORPTION OF IODINE BY ACTIVATED CARBON.

To the Editor of THE LANCET.

SIR,—The note by Mr. B. A. Adams in your issue of April 2nd (p. 724) is based on the following two assumptions, both of which, we submit, are open to considerable doubt.

1. That the prevalence of goitre is associated with the iodine content of water-supplies.

2. That water plays a material part in the supply of iodine to the human body.

The questions concerning iodine, its distribution and relationship to goitre, have recently been exhaustively studied by Dr. J. B. Orr and his co-workers at the Rowett Research Institute, Aberdeen, and two valuable reports incorporating their findings and tentative conclusions have been published by the Medical Research Council (Special Report Series No. 123, 1929, and No. 154, 1931). From these reports, which consider both the information accumulated to date from all parts of the world, and also the recent investigations by Dr. Orr in Great Britain, we learn:—

1. That analysis of the water from the supplies of a number of urban and rural areas in this country showed no correlation between the concentration of iodine in the water and the incidence of goitre in the area from which it came.

2. That the iodine content of water-supplies, especially surface waters (the most likely to be treated by activated carbon), is small compared with that of many foodstuffs.

The part generally played by drinking water in supplying iodine is very small and probably can be entirely neglected for, in a goitrous area, the deficiency of iodine in all the foodstuffs cannot be made good by that in the water, and in a non-goitrous area the amount of iodine in the water constitutes so small a proportion of the whole in all articles of diet that its absence would not be felt.

In our experience activated carbon has proved of great value in the removal of certain odours and tastes that occasionally appear in the river-derived water-supplies and which resist all other measures of treatment. In these cases, therefore, and in view of the information at present available concerning water-supplies, iodine and goitre, we are of opinion that activated carbon should not be withheld on account of its power of removing iodine. In view of the technique employed by Mr. Adams and the inaccuracy and indelicacy of all known methods for the estimation of iodine in water and foods, it is doubtful whether he is justified in arriving at the conclusion, that "all these forms of iodine were removed invariably and completely by treatment with activated carbon."

The function of a water authority is to supply an abundance of pure water which is colourless, odourless, and palatable, and the use of activated carbon may be necessary to produce these latter conditions. The supply to the human body of such essential substances as iodine, calcium, iron, vitamins, &c., is properly carried out by a well-arranged diet, and water-supplies are, as far as can at present be told, quite unimportant in these respects.

We are, Sir, yours faithfully,

JOHN F. BEALE,
ERNEST SUCKLING.

The Counties Public Health Laboratories, 91, Queen Victoria-street, London, E.C., April 8th, 1932.

THE TOLL OF THE ROADS.

To the Editor of THE LANCET.

SIR,—It might well be supposed that members of the medical profession would have a particular interest in the prevention of unnecessary death and disablement, yet from the absence of further comment on this topic since the interesting letter from Dr. Galbraith on Jan. 23rd, it must be assumed that their attitude is the same as that of the general public, which apparently may be expressed as follows: (1) The number of road accidents is not excessive. (2) In the great majority if not in all cases, pedestrians, cyclists, or other non-motorists are to blame. (3) If occasionally a motor-car is at fault it is regrettable but inevitable, and is the natural price to pay for progress.

(1) is a matter of opinion; the figures are published from time to time, and are now apparently upwards of 7000 killed and 177,000 injured per annum in Great Britain.

(2) is obviously absurd, for many accidents occur in which one or more motors alone are concerned, while many pedestrians are killed on the pavements. Further, it draws a line between motorists and pedestrians and suggests that the former are infallible, which is impossible; for motorists are merely pedestrians in a position of responsibility for which they may be quite unfitted.

As regards (3), it would be interesting to hear the views of the medical profession on the propriety of regarding the mere multiplication of the means of mechanical transport as "progress," without regard for the need for this transport or the use to which it may be put.—I am, Sir, yours faithfully,

Carlton Hill, N.W., April 6th, 1932. R. JOHN CLAUSEN.

REFERRED PAIN IN VISCERAL DISEASE.

To the Editor of THE LANCET.

SIR,—It is plain from Mr. D. Ligat's letter in your issue of April 2nd that he uses the term "viscero-sensory reflex" in a sense very different from that given to it by Mackenzie, its originator. After asking whether a viscero-sensory reflex as described by Mackenzie exists, or whether I am right in asserting that it does not exist, he quotes a passage from my book on Abdominal Pain which he believes to involve a refutation of my own argument, and remarks at the end of his quotation, "Surely Mr. Morley here postulates a true viscero-sensory reflex?" But the passage he quotes describes the splanchnic inhibitory reflex, which has nothing in common with the mechanism conceived by Mackenzie as the viscero-sensory reflex. Mackenzie defines his viscero-sensory reflex as superficial pain and hyperalgesia referred to the somatic sensory nerves of the skin and subcutaneous tissue of the abdominal wall, resulting from violent stimulation of the afferent nerve-endings in the viscera. Viscero-sensory "radiation" would have been a better term than viscero-sensory "reflex," because Mackenzie's conception was not that of a true physiological reflex arc. But I have used Mackenzie's term because it is generally understood, and I have used it strictly in Mackenzie's sense throughout. I suggest to Mr. Ligat that in discussing the validity of Mackenzie's theory he must begin by accepting Mackenzie's definition of that theory. The extract from my book that Mr. Ligat quotes is singularly unfortunate for his argument, in that it begins, "When we explore an abdomen under a general anæsthetic . . ." An unconscious patient could hardly evince Mackenzie's viscero-sensory reflex or any other pain mechanism.

I am, Sir, yours faithfully,

Manchester, April 8th, 1932. JOHN MORLEY.

THE DURATION OF THE RED LOCHIA.

To the Editor of THE LANCET.

SIR,—I have a great admiration for the work done by Dr. Remington Hobbs in the treatment of puerperal sepsis by glycerin drainage, but I feel that his efforts to establish glycerin as the panacea of nearly all obstetric and of many gynæcological conditions is being carried too far. Already to my mind it enjoys a reputation which it does not altogether deserve.

He states that prolongation of the lochia after the seventh day is due to sepsis of the uterine mucosa, and that in cases of subsequent peritonitis a history will be found of prolonged lochia for some weeks. In my experience one can fix no day between the seventh and the twelfth when the cessation of lochia can be regarded as abnormal. The amount and duration of lochia in a normal puerperium depends on the type of labour, upon bleeding during labour, and upon the size of the infant and of the placenta. Any loss after the twelfth day should be regarded as secondary post-partum hæmorrhage, and is in the vast majority of cases due to retained products, uterine displacements, tumours, and general diseases, and should be treated as such by an exploration of the uterus under anæsthesia. It is unwise to postulate the seventh day as that on which the uterus must cease its perfectly normal and beneficent drainage, and to begin manhandling it as septic is mischievous.

Again Dr. Hobbs claims, almost with pride, that out of 340 consecutive deliveries, he detected 80 as being septic. The fact that 40 were apyrexial (simply draining their uteri as Nature intended them to do) is in my opinion no indication for treatment; it is creating a disease which does not exist, and I suppose will later supply a series of statistics illustrating the curative powers of glycerin.

I am, Sir, yours faithfully,

A. MORRIS JOHNS.

Wimpole-street, W., April 7th, 1932.

USE OF TUBERCULIN IN DIAGNOSIS.

To the Editor of THE LANCET.

SIR,—The usefulness of Dr. D'Arcy Hart's report on the Value of Tuberculin Tests should certainly not be minimised, but I venture to join in the protest which is being ventilated in your columns against his condemnation of the Pirquet test. It so happens that, at an institution where I was previously assistant medical officer, a number of cases on which I had performed a Pirquet test were later tested by the Mantoux method by Dr. D'Arcy Hart. The number of cases tested by both methods was sufficient to enable me to compare the relative value of the two tests. In nearly every case the results of the Mantoux and the Pirquet agreed and were compatible with the clinical findings. Furthermore it has been my experience to see on more than one occasion a fairly marked local reaction accompanied by slight fever as a result of the Mantoux test, even in skilful hands. This has led me to prefer the Pirquet test, for any reaction which causes inconvenience to the patient is not justified in a test which may be, but is not always, of major clinical importance.

I am, Sir, yours faithfully,

M. C. WILKINSON.

Black Notley Sanatorium, Essex, April 9th, 1932.

CHRONIC DUODENAL STASIS.

To the Editor of THE LANCET.

SIR,—In the leading article on this subject in your last issue (p. 781) you refer to a paper [1] written by us two years ago in which we essayed to prove the existence of a syndrome in children owing its origin to a mild degree of duodenal obstruction from congenital arterio-mesenteric compression. Your mention of this work encourages us to state that we have recently made two additional observations which seem to support our thesis. In one case there was unequivocal evidence post mortem of congenital ileus; and in another we were fortunate enough to obtain radiographic evidence of duodenal stasis which we had hitherto failed to demonstrate. A second paper from us, dealing with this difficult subject, in which it is so necessary not to go further than the facts warrant, will appear in the April issue of the *Archives of Disease in Childhood*.

We are, Sir, yours faithfully,

REGINALD MILLER,
H. COURTNEY GAGE.

London, April 9th, 1932.

[1] Arch. Dis. Child., 1930, v., 83.

CHELTENHAM HOSPITALS.—Last year the Cheltenham General and Eye Hospitals treated 2034 in-patients to a conclusion and attended to 9756 new out-patients. The average cost of each patient treated to a conclusion was £8 6s. 11½d., and the weekly cost of each £2 16s. 4½d., a small increase. Of the income of £19,699 (deficit £674) £7400 was derived from workers' contributions.

OBITUARY

ALEXANDER L. URQUHART, M.B. Edin.,

PROFESSOR OF PATHOLOGY IN THE EGYPTIAN UNIVERSITY.

THE Faculty of Medicine of the Egyptian University has suffered a severe blow in the loss of its professor of pathology, Prof. A. L. Urquhart, whose death we announced last week.

Alexander Lewis Urquhart, son of the late Dr. A. R. Urquhart, of Perth, was born on April 15th, 1887. He was educated at Edinburgh Academy and thence proceeded in 1906 to the University of Edinburgh, where he was at first more marked out by his proficiency at games than at work, being a full exponent of football, cricket, and golf, especially the first. In 1911 he graduated as M.B., and in the same year entered the Royal Army Medical Corps. Between then and the outbreak of war he served for most of the period as demonstrator in the R.A.M.C. College at Millbank, and while thus employed he obtained the D.P.H. diploma of the Conjoint Board. Soon after the commencement of the war he was sent to France in command of a motor ambulance convoy. After a short time in this position he was transferred to the Macedonian front in charge of the main pathological laboratory, and was twice mentioned in despatches. For his services in the war he was awarded the O.B.E.

On his return to England in 1919 he was offered by Prof. L. S. Dudgeon, under whom he had worked in Macedonia, a post in the pathological department of St. Thomas's Hospital, and severing his connexion with the R.A.M.C. he accepted the offer. From then till 1927 he acted as lecturer in pathology at St. Thomas's Hospital, and Curator of the Museum. But in 1927 he was offered and accepted the chair of Pathology in the Faculty of Medicine of the Egyptian University. In this post he was an immediate success, as the following testimony from a colleague shows. "To an excellent knowledge of his subject Urquhart added the fruits of a wide and varied experience. As a teacher none could have been more patient and painstaking. He inspired his staff with an enthusiasm for teaching and research which will remain for long years as a memorial of his work in Egypt. Gentle, generous, and kindly in nature, he deeply endeared himself to all his colleagues, both English and Egyptian. His students revered him for his knowledge and repaid him with their whole-hearted affection for his devotion to them. Perhaps the most dominant feature of his character was his friendliness and his capacity for making friends. Of these, and their name is legion, each one will confess that a more sweet and lovable character could scarcely be found. His death at the early age of 44 leaves an aching void in the hearts of all who knew him."

Prof. Urquhart was not a prolific writer, but his contributions to medical literature were characterised by a very high degree of painstaking accuracy. Probably his most important articles were a review of the Serological and Morphological Characteristics of the Pneumococcus in the *Journal of the Royal Army Medical Corps* (1922) and a joint study of Bacillary Dysentery in the British Forces in Macedonia published for the Medical Research Committee.

He married in 1915 Anne, daughter of the late Mr. D. F. Addis, formerly of the Indian Civil Service. They had one son, born in 1920. He died in the evening of March 28th, and was buried, with full military honours, on the following afternoon in the British Protestant Cemetery, Old Cairo.

HENRY HARVEY, M.B. Edin.

Dr. Harvey, who has died in Liverpool in his eighty-fifth year, was widely esteemed as a practitioner in the city where he had spent most of his life. Born at Milton in Kent, the son of Jacob Harvey, he was educated at Liége in Belgium and at Edinburgh, where he qualified in 1870. He went to Liverpool in the following year as house surgeon at the Liverpool Southern and Toxteth Hospital, and at the time of his death he was the only human link between that institution and the Royal Southern Hospital to which his services were transferred on the reorganisation in 1872. On completing his resident appointment in 1873 he took up general practice in the Wavertree district, becoming medical officer of health for Wavertree, and subsequently for Childwall. As a general practitioner interested in both medicine and general surgery he was well acquainted with the professional life of Liverpool. "It is a pity," writes one of his medical friends, "that he did not write biographical sketches to place in the archives of the Liverpool Medical Institution, for he was a man of literary culture whose style was one of interesting narrative. In course of conversations with him one learnt much about the conditions, more especially of surgical practice, in the days when antiseptic surgery was in its infancy, and when faulty technique accounted for much scepticism concerning Lister's teaching. It was always interesting to meet him, because his knowledge embodied the best of the old methods of therapeusis, so many of which have unfortunately been forgotten or remain untaught, together with the modern methods of treatment in which he was well versed. He was a thoroughly sound practitioner, trusted and respected by all with whom he came in contact. His kindly, thoughtful face and gentleness of manner, together with his keen personal interest in his patients, were, in themselves, assets which promoted their well-being. Of him it might truly be said, 'He is gentil that doth gentil dedis.'"

ALEXANDER JAMES, M.D., F.R.C.P., F.R.S. Edin.

EDINBURGH has lost a distinguished physician by the death of Dr. Alexander James, at the age of 81. He belongs to the generation that included Prof. Grainger Stewart, Dr. Claud Muirhead, Prof. Wylie, and Mr. "Joe" Bell. Graduating in 1872, he studied abroad at Leipzig, and returned to become lecturer on the practice of medicine in the extra-mural school at Edinburgh. In due course he was appointed physician to the Royal Infirmary, where he was a popular clinical teacher. A colleague writes of him that he was an engaging personality and secured the devotion of his students. "He had a good speculative mind, and was ready for controversy at a moment's notice; but he made no enemies. He took strong views, but he always retained his genial temper. At the local branch of the British Medical Association and at the Medico-Chirurgical he would bring up problems like the effect of hospitals on the spread

of scarlet fever, and, on one occasion, he continued the debate over three weekly meetings." Dr. James believed that hospitals tended to spread scarlet fever, and he was strongly against the massing of children in large public schools. He opposed medical inspection of school-children by whole-time medical officers, preferring that the work should be done by the family practitioners. As he was physician to the schools of the Edinburgh Merchant Company his views led to a serious official situation. It was ultimately resolved by the company's agreement with the Scottish Education Department that the work should be done by the medical officers of the school board, and this system has been operative for over 20 years. He also had very definite views on tuberculosis, holding a theory that the Timothy grass bacillus was an active factor. He was always ready, at casual meetings, to argue the case. He was also keenly interested and well informed on sociological problems, and his occasional addresses showed that he was alive to the social aspects of medicine.

THE SERVICES

ROYAL NAVAL MEDICAL SERVICE.

Surg. Comdrs. H. M. Braithwaite and S. W. Grimwade are placed on the retd. list at their own request.

Surg. Comdr. D. H. C. Given is placed on the retd. list with the rank of Surg. Capt.

Surg. Lt.-Comdr. (D) D. Paterson is placed on the retd. list with the rank of Surg. Comdr.

Surg. Lieut. T. L. J. Barry, to be Surg. Lt.-Comdr.

The following appointments are notified: Surg. Comdrs. W. J. Colborne to *Vivid* for R.N. Hospital, Plymouth, and H. M. Whelan to *Revenge*.

Surg. Lieut. Comdr. W. P. E. McIntyre to *President*.

Surg. Lt. S. R. G. Pimm to *Penzance*.

ROYAL NAVAL VOLUNTEER RESERVE.

Surg. Lt. R. J. Matthews to be Surg. Lt.-Comdr.

Surg. Sub-Lt. R. M. Marshall to be Surg. Lt.

Proby. Surg. Sub-Lt. D. R. Hughes to be Surg. Sub-Lt.

ROYAL ARMY MEDICAL CORPS.

Maj. H. S. Blackmore, Res. of Off., R.A.M.C., relinquishes his appt. under Art. 520 (b), Royal Warrant for Pay and Promotion, 1831.

Maj. R. W. Chapman retires, receiving a gratuity.

TERRITORIAL ARMY.

Capt. H. V. Morlock resigns his commn.

Lts. C. R. L'E. Orme and J. G. Weston to be Capts.

TERRITORIAL ARMY RESERVE OF OFFICERS.

Lt.-Col. T. P. Puddicombe, having attained the age limit retires and retains his rank, with permission to wear the prescribed uniform.

INDIAN MEDICAL SERVICE.

The undermentioned officers relinquish their temp. commns.: Capts. R. C. Goulatia and S. K. Ganguli.

ROYAL AIR FORCE.

Flying Officer Hyman Ruben Clein is promoted to the rank of Flight Lieutenant.

RESERVE OF AIR FORCE OFFICERS.

Flight-Lt. J. J. Quinlan relinquishes his commission on appointment to a commission in the Indian Medical Service.

THE COLONIAL SERVICE.

Dr. E. V. W. Mellard is appointed Surgeon at Jamaica; Dr. C. H. Howat, District Medical Officer at Cyprus; Dr. J. S. Cramer, Supernumerary Medical Officer, Leeward Islands; Dr. H. B. Boucher, Medical Officer, Gambia; Dr. J. W. Murdoch, Medical Superintendent Central Mental Hospital, Federated Malay States; and Dr. A. H. Owen, Director of Medical and Sanitary Services, Tanganyika Territory.

PARIS.

(FROM OUR OWN CORRESPONDENT.)

RESTRICTION OF THE PRACTICE OF MEDICINE BY FOREIGNERS.

THE disquieting influx of foreign medical students and doctors into France, to which I have referred from time to time, has culminated in protective legislation which is likely to put a most effective barrier to future invasions of this kind. A Bill dealing with this problem was passed on Feb. 29th by the Chamber of Deputies without discussion. As it had already been approved by the Senate, there is no prospect of its being set aside. It remains, however, to be seen how far its conditional clauses will react to the circumstances of individual cases. According to the first article, no one may practise medicine in France unless he is a French subject or a native of a French Protectorate. Nor may he practise medicine without a State diploma. But in the case of those countries in which French doctors are allowed to practise, applications may be made to the French Government for dispensation in certain instances from the obligation of becoming a naturalised Frenchman. With regard to such countries, it is presumed that an equilibrium will be established in the sense that approximately as many Frenchmen as foreigners are allowed to practise in each other's countries. The second article concerns the preliminary studies and examinations which may be made obligatory on newcomers even if they already possess the medical diploma of some other country. As for the foreign medical student, the third article rules that no exemption from preliminary studies shall be made, however prolonged his studies abroad may have been. In the fourth article, surgeon-dentists with foreign diplomas are obliged, if they wish to practise in France, to pass the same examinations that are required of French students seeking a diploma in dentistry. Not more than a year of preliminary studies can be dispensed with by the would-be surgeon-dentist. As for the foreign doctors and dentists already practising in France, they must submit their diplomas for verification within three months.

AMALGAMATING EDINBURGH HOSPITALS.—A meeting of the subscribers to the Edinburgh Royal Maternity and Simpson Memorial Hospital recently unanimously agreed to the amalgamation of the institution with the Edinburgh Royal Infirmary. The agreement will require the sanction of Parliament. Last year the Simpson Hospital dealt with over 44 per cent. of the births in Greater Edinburgh, and 3467 cases were attended. The building of a new hospital on the site of George Watson's College will shortly be begun.

DONATIONS AND BEQUESTS.—Mr. Edwin Hoyle, of Old Hall Hotel, Buxton, Derbyshire, bequeathed £1500 to Ancoats Hospital and Ardwick and Ancoats Dispensary, Manchester; £1000 to St. Mary's Hospitals, Manchester; £500 to Henshaw's Institution for the Blind, Manchester; £500 to St. Dunstan's Hostel; £300 to the Devonshire Hospital, Buxton; £200 to the Dental Hospital, Manchester; £200 to Manchester and Salford Blind Aid Society; £100 to the Buxton and District Cottage Hospital; and the residue of the property as to one-fifth to the Royal National Lifeboat Institution, and four-fifths to the Manchester Royal Infirmary and Dispensary.—Mrs. Margaret Brown Cade, Kingston, left by will £1000 to Hull Royal Infirmary, and £500 to Hull and Sculcoates Dispensary.—The late Mr. Edward Brake, of Bath, left, on his wife's death, £1000 to the Royal Bath United Hospital, and £1000 to the Cancer Fund of the Middlesex Hospital, London.

PARLIAMENTARY INTELLIGENCE

NOTES ON CURRENT TOPICS.

UNEMPLOYMENT BENEFIT AND PUBLIC HEALTH.

THE House of Commons, which reassembled after the Easter Recess on Tuesday, April 5th, went the same day into Committee on the financial resolution in connexion with the Transitional Payments (Unemployed Persons) Bill. Captain BOURNE, Deputy-Chairman of Committees, was in the chair.

Sir HENRY BETTERTON (Minister of Labour) in moving the resolution, said its objects were two-fold. The first was that the power to make transitional payments to persons who had not paid 30 contributions in the past two years should be extended to June 30th, 1933; and the second was that the cost of this extension should be met by the Exchequer. Those persons who were now in receipt of transitional payments would cease to receive them so soon as their benefit period expired; and supposing that there were no new legislation they would begin to run off immediately after April 18th next. If, therefore, the power to make transitional payments beyond that date was to continue this Bill must be passed in the interim. The reason why the Bill provided that the period should be extended to June 30th, 1933, was that in June of next year the Act—or any how the material parts of it—which was passed by the Labour Government expired, and the anomalies Act passed by the Labour Government also expired on the same date. Therefore, before that time there must be new legislation dealing with the whole question. The Royal Commission set up by the Labour Government were considering what arrangements were to be made outside the insurance scheme for the able-bodied unemployed, and that must include the whole position of those now affected by transitional payments. The Bill connected with this financial resolution was therefore a temporary carrying-over measure pending legislation which would in any case be necessary next year. The cost to the Exchequer up to June 30th, 1933, was estimated to be about £20,000,000. There had been a reduction in the numbers of the unemployed of 134,000 compared with a month ago. This was the first time for over two years in which the figures had been less than they were a year before and they had to go back to December, 1929, to find a figure which was less than the corresponding period of a year ago. He thought that these figures justified the hope that when world conditions improved and economic chaos was replaced by ordered progress, this country would be among the first nations of the world to take advantage of that improvement.

OPERATION OF THE MEANS TEST.

Mr. LAWSON said that not only were the Government pushing this financial responsibility back upon the poor-law, but they were pushing it back upon the poorest families. The operation of the means test was inflicting upon great masses of the people the most disgraceful pains and penalties, amounting almost to poverty of the worst kind. He had seen a letter in the newspapers that had been received by one of the Members of the House from one of the chief doctors in one of the great hospitals of Newcastle in which there was a request that the Member should use his influence to put an end to the means test because in his own experience the doctor had had daily proof of the fact that the means test was playing havoc with the physique and the general life of the people with whom he came in contact. He (Mr. Lawson) had always been willing to give credit for the great kindness of people generally, but nevertheless he said deliberately that whether they meant it or not a great section of the well-to-do in this country had been callous concerning the application of the means test to the great masses of the people. That was the more significant when one noted that for every pound asked for on the money market it was possible to get £50 from those desirous of subscribing. After all the real problem facing the present or any other Government was to get rid of unemployment. The Government might succeed in passing this Bill, but as far as the Labour party was concerned they were in favour of ending the means test root and branch without equivocation or qualification. It was also time that the Government should realise clearly that if men could not get work it was their duty to maintain them in an adequate and decent way.

Mr. MACMILLAN said that the maintenance of the unemployed had to be carried through on economical lines now and in the future, not because any Member of the House thought that 15*s*. 3*d*. per week was a sufficient sum for a man to live upon, but because too great a strain upon public expenditure might make it impossible to pay such people any sum at all. Nevertheless it was true, whoever might be responsible for the present difficulties, that a Government which asked people to be patient under hardships must satisfy them that every step was being taken to deal with the conditions and circumstances which had made those hardships necessary. He thought that the National Government had made a good start.

THE POVERTY LINE OF SUBSISTENCE.

Mr. A. BEVAN said that they ought not to keep hundreds of thousands of people on the poverty line of subsistence. Some time ago a medical investigation was conducted in the county of Monmouth and all the children in 10 schools were examined for malnutrition. They were examined as regarded weight, for height, anæmia, poor toneless skin, lack of subcutaneous tissue, dry hair, lacking lustre, tired expression, and listless attitude. The children were compared, not with children belonging to the higher classes, but with children in the rural areas of the county. There was no difference of race. The graph for each age-group of children showed a downward curve in the schools situated in the areas where unemployment had been continuous as compared with the graph of children in the rural areas. In the age-group 11–12 years the children were on the average 4 lb. lighter in weight; in the age-group 12–13 nearly 6 lb. lighter in weight; in the age-group 13–14—children who were born when the industrial depressions tarted—the difference in weight was 7¼ lb. In every case the weight of the child was infinitely lower than the average weight for the whole country. In the matter of height the same story was told. The medical officers' report was open for public inspection and the facts spoke for themselves. The difference in height was, in some cases, half an inch, three quarters of an inch, five inches, three inches, and four inches. Yet the Ministry of Health and the Ministry of Labour said that these children were too fat and that they must sacrifice another few pounds in weight in order to keep the National Government in office.

DETERIORATION IN CHILDREN'S HEALTH.

Mr. BRIANT asked the Minister whether, considering that the present position had to continue for another 15 months, it was not possible to issue some regulations which, while not affecting the general administration of the unemployment fund, would assist its smoother operation. He believed that the means test was justified but in practice it was often found to be carried out extremely unfairly. The Charity Organisation Society was considered by some people to be rather hard, but his information from many of its most experienced members was that there was beginning to be a distinct reduction in the balance which was available for even the ordinary care of children.

He had been told of numbers of cases where there was distinct evidence of deterioration in the children's health. He was sure that this was not the wish of the Minister of Labour, but it was certainly happening. He had had complaints from private organisations which had had certain funds that they were having to spend those funds for such things as additional milk. This was a very serious thing. Further than that the action of some of the public assistance committees was such as to lead the men in the district to believe that if they got the maximum transitional benefit in no circumstances would they get poor-law relief as well. The maximum was 33*s.* 3*d.* for a man and wife and five children, and they could not live on that sum. (Hear, hear.) This condition of things would result in a dreadful deterioration in the health and physique and morale of the country and in the end the State would have to pay for that.

After further debate the resolution was agreed to.

PUBLIC HEALTH SERVICES.

On Tuesday, April 12th, on the motion that the House of Commons should go into Committee of Supply on the Civil Service Estimates, Dr. MORRIS-JONES called attention to local government administration and moved "that this House appreciates the progress made by local authorities since the passing of the Local Government Act of 1929 in coördinating and improving their public health services and, while recognising the need for economy in local expenditure, is of opinion that the development of these services should steadily continue as and when circumstances permit." After debate,

Sir E. HILTON YOUNG (Minister of Health) said that there was no foundation for the suggestion that there had been any unwise restriction of the public health services in the interests of economy. It was the policy of the Government, as it would be of any Government, to consider public health as a matter of urgent national importance, and they held that economy would be false if it resulted in reducing the efficiency of those essential services.

The motion was withdrawn.

HOUSE OF COMMONS.

TUESDAY, APRIL 5TH.

Slum Clearance.

Mr. ALBERY asked the Minister of Health if he could make a statement on the progress of slum clearance and the future intentions of the Government.—Mr. ERNEST BROWN (Parliamentary Secretary to the Ministry of Health) replied: Up to the 31st March last my right hon. friend had received resolutions declaring 408 areas in England and Wales, the clearance of which involves the displacement and re-housing of approximately 68,000 persons, to be clearance areas under the Housing Act, 1930, and 269 clearance or compulsory purchase orders had been submitted in connexion with such areas. Upwards of 13,000 houses, which are either earmarked or available for the purposes of the Act, have either been erected or are under construction. The intention is that local authorities should continue to make the fullest possible use of their powers in this matter.

WEDNESDAY, APRIL 6TH.

Hospitals and Motor Accidents.

Sir JOHN HASLAM asked the Minister of Transport if he had any information to give to the House as to the cost to the hospitals of the country during 1931 of treating motor accident cases; and what proportion of such cost had been recovered by them under the Road Traffic Act.—Mr. PYBUS replied: I regret that I am not in possession of the information asked for.

Sir J. HASLAM: Will the Minister make inquiries, because those of us who are interested in hospitals know that the receipts are infinitesimal as compared with the cost to the hospitals, and we fully expected a different state of affairs when the Bill was passed last session.

Mr. PYBUS: I am entirely sympathetic with the hon. gentleman, but as he will appreciate the information is very difficult to procure. However, I will try again.

Sir J. NALL: Could not my right hon. friend ask the police authorities to send the accident cases to the poor-law hospitals, which are in a position to make charges, rather than impose them on the voluntary hospitals.

Maternal Mortality.

Mr. RHYS DAVIES asked the Minister of Health whether the departmental committee on maternal mortality had finished their deliberations; and when would their final report be published.—Mr. ERNEST BROWN replied: My right hon. friend understands that this committee are now considering their final report, which is expected to be ready for publication towards the end of the summer.

Imports of Bacon from Lithuania.

Mr. PRICE asked the Minister of Health where the imports of bacon from Lithuania and Poland were examined; whether the bacon was imported chemically cured or smoked; and what quantity was rejected as unfit for human food in the 12 months ended Dec. 31st, 1931.—Mr. ERNEST BROWN replied: Bacon is consigned from Lithuania and Poland to Bermondsey and Hull. It may be examined there and at other ports to which it is transhipped, such as Liverpool and Newcastle. It is brine-cured, in accordance with the regulations of the Ministry of Agriculture and Fisheries. My right hon. friend regrets that he cannot state separately the total quantity of bacon from these particular countries which has been condemned.

Antenatal Clinics in London.

Mr. RHYS DAVIES asked the Minister of Health the number of antenatal clinics which had been approved by the Ministry up to date in London, the county boroughs, and the counties, giving the number of municipal and voluntary centres, the number of separate sessions in each division, and the number of sessions held on the same day as the infant consultations were held.—Sir E. HILTON YOUNG replied: The approval of my department is not now required to the establishment of antenatal clinics. The returns for the year 1930, the latest year for which complete information is at present available, show that at the end of that year the number of antenatal clinics maintained by local authorities and by voluntary associations in London, and in the county boroughs and counties in England and Wales, and the number of sessions held during the year, were as follow:—

—	Number of antenatal clinics maintained by—		Number of sessions at all antenatal clinics during 1930.
	Local authorities.	Voluntary associations.	
England—			
London	52	66	8,165
County boroughs	242	58	19,599
Counties	560	70	17,668
Totals ..	854	194	45,432
Wales—			
County boroughs	9	—	804
Counties	44 } 53		739 } 1,543
Grand totals ..	907	194	46,975

Information is not available as to the number of sessions held at the municipal and voluntary clinics, respectively, in England, or as to the number of sessions held on the same day as the infant consultations are held.

Food Consumption in Britain.

Mr. THOMAS WILLIAMS asked the Minister of Agriculture approximately the proportion of food for human consumption produced in this country and imported from abroad during 1931.—Sir J. GILMOUR replied: The latest available figures are those contained in the report on the Agricultural Output and Food Supplies of Great Britain, published by the Ministry of Agriculture and Fisheries in 1929. These estimates were based chiefly on the years 1924–27, and showed that in the case of foodstuffs (including fish) normally produced in Great Britain the value of the home production was 44·9 per cent. of the total. The comparable figure for all foodstuffs was 39·3 per cent. Similar calculations will, it is hoped, be made in connexion with the agricultural and industrial censuses for 1930, but the results cannot be available for some considerable time.

THURSDAY, APRIL 7TH.

Disability Pensions.

Major LEIGHTON asked the Minister of Labour the number of men drawing disability pension registered as unemployed at the labour exchanges.—Sir H. BETTERTON replied: At Feb. 22nd, 1932, the latest date for which figures are

available, there were 43,674 ex-Service men in receipt of disability pensions on the registers of employment exchanges in Great Britain.

Economies and the Means Test.

Mr. LOGAN asked the Minister of Labour the total amount of savings effected as a result of the working of the Anomalies Act up to the latest available date.

Mr. THOMAS WILLIAMS asked the Minister of Labour how many applications for transitional benefit had been dealt with by public assistance committees; and what was the estimated saving effected by the imposition of the means test in this connexion.—Sir H. BETTERTON replied: The weekly benefit paid to persons on the live register at the end of February, after allowing for the reduction in the rates of benefit, was about £185,000 less than would have been paid in respect of the same number of persons on the live register before the introduction of the Anomalies Regulations and the Needs Test. This saving is at the rate of about £9,500,000 a year, of which roughly £2,000,000 may be attributed to the Anomalies Regulations and £7,500,000 to the Needs Test. There was, in addition, a saving in respect of persons who, on ceasing to draw benefit or transitional payments, discontinued registration without finding employment; while it is difficult to estimate this further saving precisely, I am satisfied that the total saving is at least as much as that estimated in the White Paper (Cmd. 3952) issued in connexion with the Economy Bill. As regards the first part of the question by the hon. Member for Don Valley, between Nov. 12th, 1931, and Feb. 20th, 1932, 3,212,862 applications for transitional payments were submitted to public assistance committees in Great Britain for determination. This number included 1,421,484 initial applications, and 1,791,378 renewal applications.

Free Meals for School-children.

Mr. THORNE asked the President of the Board of Education if he had any information as to the number of children receiving free meals from the various local educational authorities throughout the country for the period Nov. 1st to the nearest available date.—Sir DONALD MACLEAN replied: During the week ended Nov. 7th last approximately 113,000 children received free meals, including milk meals, under arrangements made by local education authorities in England and Wales. For the week ended March 12th last, the latest date for which complete figures are available, the corresponding figure was 139,000.

Poor-law Relief.

Mr. LUNN asked the Minister of Health what was the total number of men and women on poor-law relief at the end of July, 1931; and what was the total at the end of March, 1932, or up to the latest date available.—Sir E. HILTON YOUNG replied: Exact figures cannot be given, but it is estimated that approximately 284,000 men and 366,000 women were in receipt of relief at the end of July, 1931, and approximately 348,000 men and 448,000 women at the end of March, 1932.

Mr. THORNE asked the Minister of Health the number of persons in receipt of poor-law relief from Oct. 1st, 1931, to March 31st, 1932.—Sir E. HILTON YOUNG replied: The returns made to my department show the number of persons in receipt of poor relief on particular days, and not the number of persons who received poor relief during a period. The following is a statement as to the number of persons in receipt of poor relief in England and Wales on the last Saturday in each month from September, 1931, to March, 1932:—

September, 1931 ..	1,005,813	January, 1932 ..	1,188,628
October, ,, ..	1,050,342	February, ,, ..	1,219,701
November, ,, ..	1,089,023	March, ,, ..	1,220,000*
December, ,, ..	1,127,006		

* Approximate.

These figures do not include rate-aided patients in mental hospitals.

Local Government.

Lieut.-Colonel ACLAND-TROYTE asked the Minister of Health whether it was proposed to introduce legislation during the present session to give effect to the final report of the Royal Commission on Local Government.—Sir E. HILTON YOUNG replied: The final report of the Royal Commission contains recommendations on a large variety of subjects. Measures have already been taken to deal with some of them. I cannot undertake to propose further legislation this session on the recommendations.

Feeble-minded Persons in Britain.

Mr. LAMBERT asked the Minister of Health the estimated number of feeble-minded persons in Great Britain; and what proportion was cared for in public institutions.—Sir E. HILTON YOUNG replied: The number of mentally defective persons, including children, was estimated by the Wood Committee to be, approximately, 300,000. On Jan. 1st, 1932, the total number of mental defectives actually ascertained by local authorities was 97,310, of whom 33,356 were in institutions or under guardianship. These figures relate only to England and Wales.

Royal Commission on Sweepstakes and Lotteries.

Mr. BERNAYS asked the Home Secretary whether he intended to institute an inquiry into the law relating to sweepstakes in this country.—Sir H. SAMUEL replied: It is generally agreed that there are serious difficulties in the way of enforcing the present law in regard to sweepstakes and lotteries. Events during the last two years have brought the matter very prominently to the attention both of the Government and the public. Questions have also arisen with regard to the use of totalisators both generally and in connexion with greyhound racing tracks. There are difficulties in connexion with the enforcement of the law relating to street betting, and from time to time new developments arise such as the attempt to introduce betting at motor-cycle speedway races. In view of the complexity of the issues involved, and the diversity of the views entertained in regard to these questions, the Government have decided that, before considering whether any amendment of the present laws is necessary, it is essential that a comprehensive inquiry should be undertaken by a Royal Commission. Steps will accordingly be taken for the appointment of a Royal Commission, with wide terms of reference, as soon as the necessary arrangements can be made.

MONDAY, APRIL 11TH.

Child Marriage in India.

Mr. MCENTEE asked the Secretary of State for India the number of prosecutions taken out under the Sardar Child Marriage Restraint Act since its enforcement; and whether legislation was being placed before the Indian legislature providing for a limitation of the scope of the provisions of the Act.—Sir S. HOARE replied: I have no information regarding the number of prosecutions instituted under the Child Marriage Restraint Act. The Government have placed no legislation before the Indian Legislative Assembly with the object of limiting the scope of the Act, but a number of such Bills have been introduced by private Members.

Indian Medical Qualifications.

Lieut.-Colonel FREMANTLE asked the Secretary of State for India whether he had approved the Bill introduced into the legislative assembly for the establishment of a medical council in India and for the maintenance of a British-Indian medical register; whether he was assured that a standard of qualification would be made and maintained which would enable such qualification to be recognised by the General Medical Council of the United Kindom; and whether medical practice both in India and in the United Kingdom and other parts of the British Empire would be freely open to medical practitioners registered by either medical council.—Sir S. HOARE replied: The answer to the first part of the question is in the affirmative. There is, I think, good reason to hope that the standard of the Indian medical qualifications recognised by the Indian Medical Council will be such as will enable them to be recognised also by the General Medical Council here. As regards the last part the present Bill does not deal directly with the right to practise in India.

Lieut.-Colonel FREMANTLE asked if the right hon. gentleman had any assurance from the General Medical Council here that they would approve the standard set up by this Bill, in which case it would settle the question?

Sir S. HOARE replied that he had had no such assurance.

Lieut.-Colonel FREMANTLE: Is it possible to get some such assurance before this Bill is passed; otherwise Indian medical men qualified in India will be debarred from practising in different parts of the Empire?

Sir S. HOARE: I could not give an answer to that question without further consideration.

Lieut.-Colonel FREMANTLE: The right hon. gentleman says he has approved the Bill. Did he consider it before he gave his approval, or is it only a temporary, provisional approval?

[No reply was given to this question.]

Danger of Polluted Shell-fish.

Sir A. MICHAEL SAMUEL asked the Minister of Health what steps were taken by authorities other than the Fishmongers' Company to safeguard consumers against the dangers of imported polluted shell-fish other than oysters.—Mr. E. BROWN (Parliamentary Secretary to the Ministry of Health) replied: Sanitary authorities have general powers for the inspection and seizure of unwholesome food, and these are put into operation from time to time to prevent the sale of shell-fish which appear to be polluted.

Sir A. MICHAEL SAMUEL asked the Minister of Health what steps were taken to require that shell-fish imported from the Irish Free State should be cleansed and sterilised

before being landed here so as to prevent their being a possible cause of typhoid if used for human consumption.—Mr. E. BROWN replied: No special regulations have been made by my department with regard to imported shell-fish, but the Irish Free State Government have made regulations prohibiting the distribution for sale for human consumption of shell-fish taken from layings in a defined area in the counties of Louth and Meath, unless the shell-fish have been washed and relaid. My right hon. friend is not aware that any similar regulations have been made applying to other layings in the Irish Free State.

Lotteries and Sweepstakes.

Sir WILLIAM DAVISON asked the Prime Minister whether it would be provided in the terms of reference to the Royal Commission which the Government purposed to set up to inquire into the law relating to lotteries, &c., that it was desirable that a report on the matter should be presented within a period not exceeding four months so that the existing anomalies of the law relating to lotteries might be remedied without delay; and whether the Government had definitely decided that, pending the Report of the Royal Commission, no facilities were to be given for the further stages of the Lotteries Bill, ordered by the House of Commons to be brought in on March 22nd.—Mr. MACDONALD replied: The terms of reference of the Royal Commission are under consideration. It would be impracticable to suggest any time limit within which the Commission are to report, but I have no doubt that they will endeavour to expedite their inquiry so far as the complexity of the issues involved will permit. It would be within the discretion of the Commission to submit interim reports should they consider it expedient to do so. Pending the receipt of their report it would be inappropriate, I think, for legislation to proceed on one aspect of the problem which they are to investigate.

Unemployed Persons and Poor Relief.

Mr. RHYS DAVIES asked the Minister of Health the proportion of persons receiving unemployment benefit and transitional benefit payments, respectively, who were also in receipt of poor relief.—Sir E. HILTON YOUNG replied: At the beginning of February, 1932, approximately 1 per cent. of the persons with claims authorised for insurance benefit, and 1·9 per cent. of those with applications authorised for transitional payments, were in receipt of poor relief. These particulars relate to England and Wales only.

Mr. RHYS DAVIES asked the Minister of Health the total number of men and women, and their dependants, respectively, receiving poor relief due to unemployment.—Sir E. HILTON YOUNG replied: During the month of February, 1932, the average numbers of unemployed men and women (and their dependants) ordinarily engaged in some regular occupation who were in receipt of poor relief in England and Wales were: men, 83,398; women, 5145; dependant wives and children, 205,499.

Mr. HORNBY asked the Minister of Labour if he was aware that owing to the action of courts of referees in disqualifying persons in the transitional class from insurance benefit many persons had had to seek public assistance, and that this number was increasing, causing a burden on the rates of many cities and towns; and whether he was prepared to promote legislation making poverty arising from unemployment a national charge.—Sir HENRY BETTERTON replied: No, Sir. I have no evidence that what my hon. friend suggests is taking place. The courts of referees have to decide, in cases of doubt and subject to appeal to the umpire, whether an applicant is normally in an insured trade; this condition has remained unchanged since transitional benefit was first instituted in 1928.

TUESDAY, APRIL 12TH.

Imports of Manchurian Partridges.

Mr. J. P. L. THOMAS asked the Minister of Health whether he was aware that Manchurian partridges were being imported at the present time into Great Britain; and whether he was satisfied that the conditions under which these birds were trapped and transported were such that their sale in this country complied with the provisions governing the purity of food-supplies.—Mr. E. BROWN replied: My right hon. friend understands that very few of these birds have been imported recently into this country. He has no definite information as to the conditions under which they are trapped and transported, but they are subject to inspection at the ports in this country under the Public Health (Imported Food) Regulations.

COTTAGE HOSPITAL COSTS.—Last year the Lyme Regis and District Cottage Hospital admitted 188 in-patients who cost on the average £3 15*s* 1½*d*. per week, a reduction of 5*s*. 6*d*. on the preceding years.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED APRIL 2ND, 1932.

Notifications.—The following cases of infectious disease were notified during the week:—Small-pox, 95 (last week 41); scarlet fever, 1435; diphtheria, 815; enteric fever, 19; acute pneumonia (primary or influenzal), 1662; puerperal fever, 49; puerperal pyrexia, 104; cerebro-spinal fever, 69; acute poliomyelitis, 5; acute polio-encephalitis, 1; encephalitis lethargica, 16; dysentery, 15; ophthalmia neonatorum, 96. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on April 5th–6th was as follows: Small-pox, 121 under treatment, 4 under observation (last week 115 and 10 respectively); scarlet fever, 1390; diphtheria, 1432; enteric fever, 12; measles, 2757; whooping-cough, 435; puerperal fever, 30 (plus 13 babies); encephalitis lethargica, 226; poliomyelitis, 4; "other diseases," 131. At St. Margaret's Hospital there were 8 babies (plus 5 mothers) with ophthalmia neonatorum.

Deaths.—In 117 great towns, including London, there was 1 death from small-pox, 2 (1) from enteric fever, 114 (65) from measles, 4 (2) from scarlet fever, 46 (7) from whooping-cough, 30 (5) from diphtheria, 51 (9) from diarrhœa and enteritis under two years, and 158 (27) from influenza. The figures in parentheses are those for London itself.

Worcester reports the only death from enteric fever outside London. The fatal case provisionally classified to small-pox occurred in Deptford Metropolitan Borough. Deaths from influenza are sharply declining, the largest total being reported from Bristol with 13, followed by Sheffield with 7. Ten of the fatal cases of measles were reported in Liverpool, 5 each in West Ham and Portsmouth. There were 4 deaths from whooping-cough in West Ham and in Liverpool. Diphtheria accounted for 5 deaths in Liverpool, 4 in Hull.

The number of stillbirths notified during the week was 313 (corresponding to a rate of 47 per 1000 births), including 51 in London.

FATAL CASE OF SMALL-POX.—This case which occurred in Deptford was, Dr. F. L. Keith tells us, that of an unvaccinated infant, 3 weeks old at death. The child was infected during the first three days after birth, contracting the disease from her sister who had been in contact with other cases at school. The cause of death was given in the certificate as (*a*) pyæmia, (*b*) small-pox.

WALSALL CONTRIBUTORY SCHEME.—Under the terms of the contributory scheme which it is proposed to establish for Walsall General Hospital the following are eligible for membership: (1) married persons whose income does not exceed £312 per annum; (2) unmarried persons, widows, and widowers whose income does not exceed £250; (3) unmarried persons, widows, and widowers, whose income does not exceed £312, but who have relatives dependent on them; (4) young persons between the age of 14 and 16. Dependents of Classes 1 and 3 are also eligible for treatment. The contributions in Classes 1 and 3 are 3*d*. per week; Class 2, 2*d*. per week; Class 4, 1*d*. per week. Employers are invited to add a subscription of not less than one-third of their employees' contributions. The hospital's present income is £15,000, it spends £18,000, and needs £20,000.

ORTHOPÆDIC HOSPITALS.—At the Manfield Orthopædic Hospital, Northampton, the average stay of a patient last year was 232 days at a cost of £83 13*s*. 8*d*. Dr. J. M. Mackintosh, the county medical officer, states that 70 per cent. of the patients become wage earners, and that "the quality of the treatment and the nursing are unsurpassed in this country."—The Wingfield Orthopædic Hospital at Headington, Oxford, which serves Berkshire, Buckinghamshire, and Oxfordshire, has been renamed the "Wingfield-Morris" Hospital in recognition of the generosity of Sir William Morris in undertaking to defray the entire cost (£70,000) of the new building. The old hospital consisted of temporary wooden buildings. The reconstruction scheme includes 140 beds, nurses' quarters with 50 rooms, a trainees' hostel for 22, and complete new workshops.

MEDICAL NEWS

University of Oxford.

The George Herbert Hunt travelling scholarship for 1932 has been awarded to John Charles Leedham-Green, B.M.

Next June there will be an election to the Schorstein Research Fellowship in Medical Science. The Fellowship, of the annual value of £200, will be tenable for two years from Oct. 1st in any of the medical departments at Oxford. Candidates must be graduate members of the University, holding a registrable medical qualification, and must be under 35 years of age on Oct. 1st. They must submit their applications, in proper form, to the Dean of the Medical School, University Museum, not later than May 2nd.

University of London.

At University College Dr. C. S. Myers, F.R.S., will deliver the Hobhouse memorial lecture on the Absurdity of any Mind-Body Relation, at 5.30 P.M. on Thursday, May 19th. Three lectures on Human and Comparative Placentation, including the Early Stages of Human Development, will be given by Dr. Otto Grosser, professor of anatomy in the German University, Prague, at 5.15 P.M. on May 2nd, 5th, and 6th. Dr. W. R. Hess, professor of physiology in the University of Zurich, will deliver two lectures on the Autonomic Nervous System at 5.30 P.M. on May 12th and 13th.

The Senate will shortly consider applications for grants from the Thomas Smythe Hughes and Beaverbrook Medical Research Funds for the assistance of original medical research. Applications must be received in proper form not later than May 15th. Applications are also invited for the Laura de Saliceto studentship for the advancement of cancer research, which is of the value of £150 a year. Further particulars of the grants and studentship may be had from the Academic Registrar.

Our advertisement columns contain particulars of the Geoffrey Duveen travelling studentship for research in oto-rhino-laryngology, for which application is invited.

University of Birmingham.

The Ingleby lectures will be given in the Edmund-street Buildings at 4 P.M. on Thursdays, May 5th and 12th, by Prof. Seymour Barling, whose subject will be the Operative Treatment of Toxic Goitre. As already announced, the Withering lectures, on Some Aspects of Human Biology, will be given by Mr. C. J. Bond, at the same hour and place, on Wednesdays, April 20th and 27th, and May 4th, 11th, and 25th.

Hunterian Society.

The next award of the Society's gold medal will be made in 1932 for the best essay received on or before Dec. 31st. The competition is open to all general practitioners resident in Great Britain, Ireland, and the Channel Islands, and for this purpose the council define a general practitioner as one who is not established in a special branch of work or in consulting practice. The rules governing the award may be obtained from the secretary, Mr. Andrew McAllister, 79, Wimpole-street, W.1.

More Money than Patients.

Prudhoe Memorial Convalescent Home, Whitley Bay, Northumberland, has a credit balance of £936 but lacks a sufficiency of inmates, the number, entirely men, having fallen by 150 to 1007. The reasons given are the straitened resources of employers, workmen's societies and clubs, and the opening of the home at Conishead Priory for miners in the county of Durham. A subscriber of £2 2s. is entitled to send a convalescent for three weeks although the cost to the Home is £4 10s. 2d.

National Birth Control Association.

This association, with which is incorporated the Birth Control Investigation Committee, will hold a medical conference at the Caxton Hall, London, from May 20th to 22nd. The subject of the meetings and the names of the chairmen are as follows: Friday, May 20th, 2.30 P.M., Spermotoxins and Hormones (Sir Thomas Horder); May 21st, 10.30 A.M., Spermicidal Preparations and their Effects (Dr. C. P. Blacker); May 21st, 2.30 P.M., Methods at Present in use at Clinics (Dr. Killick Millard); May 22nd, 10.30 A.M., the Gräfenberg Ring and other Methods (Sir Humphry Rolleston). It is stated that the members of the conference will be medical officers of health and members of their staffs, research workers, doctors in hospitals and in private practice, and doctors and a few lay workers from the voluntary clinics. Particulars may be had from the secretary of the association at 25, Eccleston-street, London, S.W.1.

Royal Faculty of Physicians and Surgeons of Glasgow.

Sir D'Arcy Power will deliver the Finlayson memorial lecture in the Hall of the Faculty, 242, St. Vincent-street, Glasgow, at 4 P.M., on Thursday, April 21st. His subject will be the Progress of Surgery in a London Hospital, 1880–1930, and all medical practitioners are invited to attend.

Indian Medical Service Dinner.

The annual dinner of the Indian Medical Service will be held at the Trocadero Restaurant, London, on Wednesday, June 15th, at 7.15 P.M. Major-General J. W. D. Megaw has been invited to take the chair. Tickets and all particulars may be had from the joint honorary secretary, Major Sir Thomas Carey Evans, Hammersmith Hospital, Ducane-road, London, W. 12.

Post-graduate Course for Ship Surgeons.

The first part of a course for ship surgeons has just begun in London under the auspices of the Seamen's Hospital Society, Greenwich. Further sections of the course will be held in the summer and autumn.

Post-graduate Course in Tuberculosis.

Under the auspices of the tuberculosis department of the Welsh National School of Medicine, and the Welsh National Memorial Association, a week's post-graduate course in tuberculosis will be held in Cardiff from June 1st. The provisional programme may be had from the hon. secretary for post-graduate courses, Joint Tuberculosis Council, 8, Highway-court, Beaconsfield, Bucks.

New Tuberculosis Clinic in Manchester.

On April 4th the Lord Mayor opened the new tuberculosis dispensary, or clinic, as it is to be called in future, which the Manchester public health committee has built opposite the Royal Infirmary. It will be the administrative centre of the tuberculosis scheme. The building has cost £22,000.

John Abernethy in a Broadcast Play.

A play about Dr. John Abernethy, written by Mr. Rudolph de Cordova and his wife, Miss Alicia Ramsey, is to be the first play broadcasted from the new Broadcasting House in London on May 2nd and 3rd. It was given over the wireless four times last year.

Torbay Hospital.

Last year this hospital admitted 2097 patients, as against 1941 in 1930 and 1668 in 1929; their average weekly cost was £2 18s. 4d., and their average stay 22·4 days. Of the total ordinary income of £20,000 the contributory scheme provided £5685.

Anglo-Yugoslav Hospital, Belgrade.

Dr. Katherine Macphail, founder and medical superintendent of this hospital, states that children are being turned away nearly every day owing to lack of accommodation. This is one of the consequences of the closing of 20 out of the 50 beds owing to the reduction of support given by English friends of Serbia through the Save the Children Fund, which makes a special appeal for funds to maintain the work. Gifts may be sent to Mr. H. D. Watson, chairman and hon. treasurer, 40, Gordon-square, London, W.C.1.

Royal Microscopical Society.

At a meeting of this society to be held at the B.M.A. House, Tavistock-square, London W.C., at 4 for 5 P.M., on Wednesday, April 20th, Mr. Conrad Beck, the president, will open a discussion on the Microscopy of the Filtrable Viruses. He will be followed in the discussion by Mr. J. E. Barnard, F.R.S., Prof. J. C. G. Ledingham, F.R.S., Dr. S. P. Bedson, Mr. C. C. Hurst, Prof. J. McIntosh, Capt. S. R. Douglas, F.R.S., Mr. W. J. Elford, Dr. G. M. Findlay, Mr. B. K. Johnson, and others.

Hospital Visiting Days.

It is proposed to limit the visiting of patients in the Manchester municipal hospitals to three afternoons a week, and to issue only three visiting permits to the relations or friends of each patient. Hitherto visits could be paid every afternoon, and visiting has grown to such an extent as to interfere with the work of the wards. It is found that so many and such frequent visitors disturb the patients, retard their recovery by the discussion of "home worries," hinder the training of nurses, and make the wards dirty, while visitors are often persons whom the patients do not wish to see. On a recent afternoon 1300 visitors entered an institution in 70 minutes while on a Saturday the number exceeded 1800.

Medical Diary

Information to be included in this column should reach us in proper form on Tuesday, and cannot appear if it reaches us later than the first post on Wednesday morning.

SOCIETIES.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.

TUESDAY, April 19th.—5 P.M., SPECIAL MEETING OF FELLOWS. To consider the proposed change in By-law 1, 7b. 5.30 P.M., GENERAL MEETING OF FELLOWS. 8 P.M., EPIDEMIOLOGY AND STATE MEDICINE. DISEASE IN CHILDREN. Special discussion on Infection in the Dormitory. Openers: Dr. J. A. Glover and Dr. R. E. Smith, Epidemiology; Surgeon-Capt. S. F. Dudley and Dr. W. H. Bradley, Disease in Children. Other speakers will take part. Members of the Section of Medicine are specially invited to attend.

THURSDAY.—7.45 P.M., NEUROLOGY. A clinical meeting t the National Hospital, Queen-square, W.C. 8.30 P.M., UROLOGY. Paper: Dr. Hugh Cabot (Mayo Clinic, Rochester, U.S.A.): Nephrostomy in Theory and Practice. Illustrated by diagrams and lantern slides.

FRIDAY.—8 P.M., EPIDEMIOLOGY AND STATE MEDICINE. Dr. A. S. M. Macgregor: Puerperal Fever and Pyrexia.

CHELSEA CLINICAL SOCIETY.

TUESDAY, April 19th.—8.30 P.M. (at the Hotel Rembrandt, Thurloe-place, S.W.), Wing-Commander H. A. Treadgold, R.A.F., will open a discussion on Physical Fitness and Aviation. The Meeting will be preceded by Dinner at 7.15 P.M. for 7.30 P.M.

ROYAL MICROSCOPICAL SOCIETY.

WEDNESDAY, April 20th.—5 P.M. (at B.M.A. House, Tavistock-square, W.C.), Discussion on the Microscopy of the Filtrable Viruses.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.

MONDAY, April 18th, to SATURDAY, April 23rd.—CENTRAL LONDON THROAT, NOSE, AND EAR HOSPITAL, Gray's Inn-road, W.C. Clinical Course in Diseases of the Ear, Nose, and Throat, occupying the whole of each day. Special (limited) classes in Operative Surgery, Pathology, Peroral Endoscopy.—LONDON LOCK HOSPITAL, 91, Dean-street, W. Afternoon course in Venereal Disease. (The above courses are open only to Members.) Further particulars from the Fellowship of Medicine.

WEST LONDON HOSPITAL POST-GRADUATE COLLEGE, Hammersmith-road, W.6.

MONDAY, April 18th.—10 A.M. to 1 P.M., Gynæcological Ward, Surgical Wards. Genito-Urinary Operations, Skin Department. 2 to 4 P.M., Operations, Surgical Wards. Medical, Surgical, Gynæcological, and Eye Out-patients. 4.15 P.M. (Lecture), Mr. Sinclair: Acute Appendicitis.

TUESDAY.—10 A.M. to 1 P.M., Medical Wards, Surgical Demonstration, Throat Operations, Dental Department. 2 to 4 P.M., Operations, Medical, Surgical, and Throat Out-patients. 4.15 P.M. (Lecture): Dr. Owen: Infant Feeding.

WEDNESDAY.—10 A.M. to 1 P.M., Medical Wards, Children's Medical Out-patients. 2 to 4 P.M., Gynæcological Operations, Medical, Surgical, and Eye Out-patients. 4.45 P.M., Venereal Diseases Demonstration.

THURSDAY.—10 A.M. to 1 P.M., Neurological Out-patients, Fracture Demonstration. 2 to 4 P.M., Operations, Medical, Surgical, Genito-Urinary and Eye Out-patients. 4.15 P.M. (Lecture): Mr. Roche: The Investigation of a Urinary Case.

FRIDAY.—10 A.M. to 1 P.M., Medical Wards, Skin Out-patients, Dental Department. 12 noon, Medical Lecture. 2 to 4 P.M., Operations, Medical, Surgical, and Throat Out-patients. 4.15 P.M. (Lecture): Dr. Owen: Infant Feeding.

SATURDAY.—9 A.M. to 1 P.M., Throat Operations, Medical and Surgical Wards, Surgical and Children's Medical Out-patients. The lectures at 4.15 P.M. on Mondays, Tuesdays, Thursdays, and Fridays are open to all medical practitioners without fee.

ROYAL SOCIETY OF ARTS, John-street, Adelphi, W.C.

MONDAY, April 18th.—8 P.M., Prof. J. C. Drummond: Recent Researches on the Nature and Function of Vitamins. (First of three lectures.)

ROYAL INSTITUTION, Albemarle-street, W.

FRIDAY, April 22nd.—9 P.M., Prof. J. B. S. Haldane: Hereditary Transmission of Acquired Characters.

ST. PAUL'S HOSPITAL, Endell-street, W.C.

WEDNESDAY, April 20th.—4.30 P.M., Mr. H. P Winsbury White: Diagnosis and Treatment of Surgical Diseases of Urinary Tract in Children.

ST. PETER'S HOSPITAL, Henrietta-street, Covent Garden, W.C.

WEDNESDAY, April 20th.—3 P.M., Mr. R. O. Ward: Diagnosis and Treatment of Vesical Papillomata.

ST. MARK'S HOSPITAL, City-road, E.C.

THURSDAY, April 21st.—4.30 P.M., Mr. J. P. Lockhart-Mummery: Treatment and Prognosis; Cancer of the Rectum.

MANCHESTER ROYAL INFIRMARY.

TUESDAY, April 19th.—4.15 P.M., Mr. A. H. Burgess: Back Pressure in Surgery.

FRIDAY.—4.15 P.M., Dr. D. E. Core: Demonstration of Medical Cases.

SALFORD ROYAL HOSPITAL.

THURSDAY, April 21st.—Mr. L. D. Mercer: Demonstration of Aural Cases.

WESTERN INFIRMARY, Glasgow.

WEDNESDAY, April 20th.—4.15 P.M., Dr. John Gracie: Medical Cases.

UNIVERSITY OF BIRMINGHAM.

WEDNESDAY, April 20th.—4 P.M., Mr. C. J. Bond: Some Aspects of Human Biology. (First of five William Withering memorial lectures.)

Vacancies

For further information refer to the advertisement columns.

Altrincham General Hospital.—Jun. H.S. At rate of £120.

Barrow-in-Furness, North Lonsdale Hospital, —H.S. £175.

Barry U.D.C. Surgical Hospital.—H.S. £200.

Beckenham, Kent, Bethlem Hospital, Monk's Orchard, Eden Park. Res. H.P. At rate of £200.

Birmingham, Dudley-road Hospital.—Jun. Asst. Res. M.O.'s. At rate of £200.

Blackburn Royal Infirmary.—Res. H.P. £175.

Brighton, Royal Sussex County Hospital.—H.P. £150.

Burton-on-Trent, General Infirmary.—Cas. O. and H.P. £150.

Canterbury, Kent and Canterbury Hospital.—H.P. At rate of £125.

Charing Cross Hospital, W.C.—Res. Cas. O. £200.

Chester, East Lancashire Tuberculosis Colony, Barrowmore Hall, Gt. Barrow.—H.P. At rate of £100.

Cobham, Surrey, Schiff Home for Recovery.—Res. Surgeon. At rate of £200.

Colchester, Essex County Hospital.—Asst. H.S. £120.

Derby, Derbyshire Hospital for Sick Children.—Res. H.S. At rate of £130.

Durham County Hospital.—Two H.S.'s. Each £150.

Ealing Borough.—Asst. M.O.H. £600.

Elizabeth Garrett Anderson Hospital, 144, Euston-road, N.W.—Pathologist. £300.

Evelina Hospital for Sick Children, Southwark, S.E.—Hon. Phys. to Out-patients.

Folkestone Borough.—Asst. M.O.H. £600.

Hampstead General and North-West London Hospital, Haverstock-hill, N.W.—H.S. £100.

Hastings, Royal East Sussex Hospital.—Sen. H.S. At rate of £150.

Hospital for Sick Children, Great Ormond-street, W.C.—Secretary. £750.

Hull Royal Infirmary.—H.P. for Sutton Branch Hospital. At rate of £160.

Ilford, King George Hospital.—Two H.S.'s. Each at rate of £100.

Ipswich, East Suffolk and Ipswich Hospital.—H.S. £120.

Isleworth, West Middlesex County Hospital.—Ophthalmic Surgeon. 3 gns. per session.

Leeds Hospital for Women.—H.S. At rate of £100.

Leeds Maternity Hospital, Hyde-terrace.—Sen. H.S. and Jun. H.S. At rate of £52 and £26 respectively.

London Light and Electrical Clinic, Ranelagh-road, S.W.—Hon. Manipulative and Electrical Clinic.

London University.—University Chair of Physiology. £1100.

Manchester, Royal Children's Hospital, Pendlebury.—Res. M.O. At rate of £125.

Minehead, Somerset, Minehead and West Somerset Hospital.—Res. M.O. At rate of £150.

National Temperance Hospital, Hampstead-road, N.W.—Hon. Asst. Phys.

Newcastle-upon-Tyne Hospital for Sick Children.—H.P., Sen. H.S., and Jun. H.S. Each at rate of £100.

Newcastle-on-Tyne, Royal Victoria Infirmary.—Jun. Surg. Reg. £150.

Northampton General Hospital.—H.S. to Ear, Nose and Throat Department. At rate of £150.

Portsmouth, Royal Hospital.—Cas. O. At rate of £100.

Preston and County of Lancaster Royal Infirmary.—Cas. O. At rate of £150.

Queen's Hospital for Children, Hackney-road, E.—Clin. Asst. for Med. Out-patients. 5s. each attendance.

Radcliffe-on-Trent, Notts, County Mental Hospital.—Second Asst. M.O. £450.

Reading, Royal Berkshire Hospital.—H.P., Cas. O., and Res. M.O. Each at rate of £150.

Retford, Notts, Rampton State Institution.—Fourth M.O. £400.

Royal Northern Hospital, Holloway, N.—H.P. At rate of £70.

St. John's Hospital, Lewisham, S.E.—Cas. O. At rate of £100.

St. Olave's Hospital, Lower-road, Rotherhithe, S.E.—Res. H.P. At rate of £80.

St. Thomas's Hospital, London, S.E.—Chief Asst. to Ophth. Dept.

South London Hospital for Women, Clapham Common, S.W.—H.S. At rate of £100.

University College, Gower-street, W.C.—Bayliss-Starling Memorial Scholarship. £120.

Walsall General Hospital.—Res. Surg. O. At rate of £300.

Wealdstone Parish,—District M.O. £100 Also Public Vaccinator.

Wrexham and East Denbighshire War Memorial Hospital.—Res. H.S. At rate of £150.

York, North Riding Mental Hospital.—Temporary M.O. 7 gns. per week.

The Chief Inspector of Factories announces vacancies for Certifying Factory Surgeons at St. Just (Cornwall); Easingwold (Yorks, North Riding); Hornsea (Yorks, East Riding); Sutton-in-Ashfield (Notts); and Haslemere (Surrey).

NOTES, COMMENTS, AND ABSTRACTS

THE CIGARETTE HABIT.

AT a meeting of the Society for the Study of Inebriety on April 12th, with Lady BARRETT, the President, in the chair, Dr. J. D. ROLLESTON surveyed published reports on the effects of cigarette smoking. Cigarettes, he said, had not been smoked in England to any large extent until after the Crimean war, and women had not adopted the habit until late in the last century when ladies of the demi-monde had first taken to smoking. The habit had increased considerably at the time of the late European war, and it had been estimated that in America $922,500,000 was spent annually on cigarettes—a sum sufficient to build two and a half Panama canals. The percentage of nicotine in cigarette smoke was about half that in cigar or pipe smoke, but it contained a relatively large proportion of carbon monoxide, which was capable of producing the symptoms of mild carbon monoxide poisoning in persons who smoked more than 20 cigarettes a day. Cigarettes also contained traces of pyridine and furfural.

The process of cigarette smoking was rhythmical, soothing, and pleasant, but it was unquestionably a drug habit. There was no evidence in support of the popular view that cigarette smoke was antiseptic, and decay of teeth might progress in the mouths of heavy smokers. The habit reduced appetite and affected health, and was, in the view of some observers, one of the factors responsible for the increase of tuberculosis in young girls. There was also evidence to show that it was often associated with gastric or duodenal ulcer. The effect of cigarette smoking on the respiratory system was a local irritation affecting the pharynx, larynx, and trachea. Hildebrand attributed to the habit chronic bronchitis, spasm of the bronchi with bronchial asthma, and relaxation of the muscles of the bronchi. These results were quite likely to develop in non-smokers who were constantly in a smoky atmosphere. The effects of excessive smoking on the cardio-vascular system were increase in the pulse-rate, palpitation, arrhythmia, rise of blood pressure, and cardiac neuroses, with occasional development of the symptoms of angina pectoris. Few observations on the blood of heavy smokers had been recorded, but one case had been reported of a leech which, after tasting the blood of such a patient, had fallen off and died in convulsions. Nervous symptoms included tremor, giddiness, headache, and insomnia. Conjunctivitis sometimes occurred, but amblyopia was rare in cigarette smokers. The relation between cigarette smoking and cancer was debatable; it was thought by some to play the part of a chronic irritant in the production of leucoplakia of the lips and tongue. Cancer of the lung was increasing in incidence and was said to be relatively frequent in waiters and innkeepers who worked in a smoky atmosphere. Opinion was fairly unanimous that smoking was deleterious to young persons, and in America some attempt had been made to demonstrate a connexion between delinquency in children and cigarette smoking. He quoted the opinion of two observers that the allowance for an adult should be five cigarettes a day.

Sir ROBERT ARMSTRONG-JONES mentioned the case of some boys admitted to Claybury with mental symptoms following on the anæmia induced by excessive smoking. Smoking induced a passive, suggestible state in which images might be regarded as realities. On the other hand, cigarette smoking might act as an antidote to a disturbed mental state, and the London County Council had recently decided to spend a large sum yearly on tobacco for use in their lunatic asylums. He agreed that it was better that young or highly strung persons should not be allowed to smoke.

Dr. A. P. CAWADIAS pointed out that as the smokers far outnumbered the non-smokers, there must always be a preponderance of smokers among a group of patients suffering from any disease. Tobacco smoking, however, certainly had the effect of raising the blood cholesterol, and in some patients this tended to produce changes in the arterial walls and endarteritis obliterans. In another group of patients tobacco acted on the sympathetic nervous system and gave rise to gastro-intestinal symptoms. Cigarette smoking might be valuable in some cases, soothing the nervous system; in others it was deleterious.

Mr. W. MCADAM ECCLES pointed out that intermittent claudication was rare except in Polish Jews, and that cigarette smoking was widespread, so that some individual factor was probably operative in this condition. Gastric ulcer had at one time been common in young women, owing, he considered, to septic teeth. Nowadays it was less common in young women and much commoner in young men; he believed that cigarette smoking was partly responsible for the increase, coupled with the fact that young women took more care of their teeth than young men.

Dr. W. M. FELDMAN described a case of suspected pyloric stenosis in an infant whose mother was a heavy smoker. No signs of pyloric stenosis were found on examination, and he suspected nicotine poisoning; anlaysis of the mother's milk, however, revealed not a trace of nicotine. He suggested that the cigarette habit and delinquency in children might both spring from some common cause instead of standing in the relation of cause and effect.

Prof. LEONAR FINDLAY asked why the increase of cigarette smoking in women should be associated, in them, with a reduction in the incidence of gastric ulcer. He thought the worst harm attributable to cigarette smoking was an irritation of the upper air passages, and he was not astonished that it should be deleterious to tuberculous patients for that reason.

THE PREVENTION OF SCHISTOSOMIASIS.

SCHISTOSOMA infection, widespread in the tropics, is of two sorts, due to *S. hæmatobium*, which attacks mainly the genito-urinary system, or to *S. mansoni*, which attacks the rectum. The ova in water develop miracidia, which in suitable water-snails encyst themselves and give rise to free-swimming cercariæ. These perforate the skin of people who wade or wash in water, or the intestinal mucosa of people who swallow them in drinking; and in the human body they achieve their sexual stage. Prevention, apart from general hygiene, is by destruction of the water-snails particularly involved. These intermediate hosts are not yet in all areas certainly identified, and to their discovery in Liberia and French Guinea Dr. Hans Vogel,[1] of the Hamburg Tropical Medicine School, has devoted much skill and energy. Working at the Bolahun Missionary Hospital in the north of Liberia in the rainy season (April to September) of 1930 he found that some 40 per cent. of the natives were infected with *S. hæmatobium*, and that the intermediate host was unknown. *Physopsis globosa* is believed to be the carrier in neighbouring Sierra Leone, but no cercariæ came from the physopsis examined in Liberia, nor would miracidia attack physopsis there (480 snails examined). As to *S. mansoni*, which causes infection in Liberia but rarely, the cases seen are mostly in immigrants. Dr. Vogel made two trips to the near-by French native town, Tamassodou, where *S. mansoni* infection was rife. He had difficulty in obtaining fæces for examination, but children, tempted by ices, would coöperate. Of 81 persons examined, 75 (over 90 per cent.) were infected, and this great difference was explained when, almost at once, he found a water-snail, new to the area, *Planorbis pfeifferi*, which carried *S. mansoni*, a small shell like an

[1] Arch. f. Schiffs- u. Trop.-Hyg., March, 1932, p. 108.

ammonite, ½ inch across, not found in Liberia, and he had had it identified by Prof. Degner in Hamburg and by Major M. Connolly in London. The town is, he tells us, near the top of a hill, and below in the valley is a rice farm. On the way to this is an area used as the general latrine, lying at the head of a small brook which carries fæces, &c., to the stream below. This brook enters at the top of a half-mile reach, which he found had been selected by reason of its nearness, its open access and sunlight, and its gentle current, for the watering, washing, and bathing activities of the village women and children. The same physical advantages, and the fæcal contamination, make the reach also a favourite for water-snails. In a couple of hours Vogel got 517 *Physopsis globosa* and 178 *Planorbis pfeifferi* from the reach; the physopsis had no *mansoni* cercariæ, but the planorbis had; and planorbis, kept a time in quarantine to prove they were uninfected, were greedily attacked by miracidia from a monkey infected by *S. mansoni*, with resulting sporocyst formation. The monkeys had been infected either orally or through the skin, and their fæces, tested by the Teleman method, showed *S. mansoni* ova in 40–50 days, while male and female worms were found post mortem in the portal and other veins. Vogel recommended that a new channel be dug for the stream to sidetrack "the reach" and kill its snails by drying, and that new watering-places be made free from planorbis. Bridges or plank roads over swamps would reduce infections, he says, but better arrangements for latrines are most chiefly needed. Specific mass treatment of natives will, he thinks, do little good until these other measures are in train.

ANIMALS IN CAPTIVITY.

THE opening of the zoological park at Whipsnade last May has given the Zoological Society of London a magnificent opportunity of showing what can be done to maintain the health of wild animals in captivity. Last summer was not all that it should have been and the winter has had severely cold spells, but the majority of the animals at Whipsnade have thrived in all weathers. Two pigmy hippopotamuses from tropical West Africa, which spent several weeks in one of the large paddocks with no artificial heat, put on weight and grew hair on their bodies. An elephant also grew abundant hair on its back. A number of animals at Whipsnade have signified their response to the healthy life by breeding, among them yaks, llamas, red and fallow deer, wallabies, muntjacs, and even wolves. The policy at Whipsnade has been to allow all the animals the greatest possible amount of space and liberty, with the result that the public has made some complaint that few animals are to be seen. This is now being rectified partly by the animals already there becoming so tame as to be easily visible, partly by the steady development of accommodation for others; there is already one den for lions in a reinforced chalk quarry, and a large enclosure of rough scrub is being fenced in to serve as a second den. Colonies of European and Canadian beavers have been introduced into three small permanent ponds, and some February swamps are being made permanent by puddling the flooded ground. Barley left standing on five acres affords cover for pheasants, partridges, and ground game, while the foxes which it was deemed prudent to evict when the park was enclosed are apt to return and make depredations on more peaceable inmates. Grey squirrels and rats have been destroyed, and numberless rabbits are transferred to the larder of the London gardens.

The health record at Regent's Park also is increasingly good. Last year only one monkey died of tubercle, and it was probably already infected on arrival. A kangaroo which died of tubercle in the pancreas was found by Dr. Stanley Griffith to harbour the avian type of bacillus. Enteritis, regarded as a good indication of the standard of cleanliness and general sanitation, falls steadily from year to year. Cat distemper only affected three recently imported leopard cubs, an immunity no doubt due in part to the provision of a new isolation ward. Rickets in young monkeys is being treated with increasing success with cod-liver oil and sun rays, but evidence is growing to show that the disease in civets and genets is not of the same character, and does not yield to the usual antirachitic treatment. Only one cancerous growth was found during the year—namely, a kidney tumour in a hamster. Kidney disease with dropsy is not an uncommon cause of death in elderly carnivores. Respiratory diseases being primarily climatic are found more difficult to control, and remain fairly constant; but speaking generally, the period required for acclimatisation has been steadily reduced. Finally, we should not overlook the service rendered to the eyes of sundry beasts by Miss Ida Mann, who removed a senile cataract from a Capuchin monkey, and needled the lens capsule of a young lemur with congenital cataract, with recovery of sight in each case. Altogether the zoo, old and new, affords the visiting public many useful lessons by analogy in adaptation to environment.

THE LADY CHICHESTER HOSPITAL.

THIS hospital at Hove, which is designed to receive cases of early nervous breakdown, had 45 patients in residence at the end of 1930, while its out-patient department saw 1778 patients during the year. Increasing demands upon the hospital have necessitated further extension, and a new department for men has been opened in coöperation with the Royal Sussex Hospital. There are now eight beds for men, 47 for women, and six for children. The financial position of the hospital causes great anxiety, but the demand for treatment is always greater than the available supply. Patients are put to bed at first and given plenty of rest, good food, fresh air, and sunlight. Occupational therapy, both in organised forms and by means of amusements and hobbies generally, forms a very important part of the treatment. Toxic foci are sought and eliminated, and hydrotherapy, massage, and electrical treatment are found valuable. A useful development has been the establishment of a system of "daily out-patients"—patients who spend their day at the hospital, but sleep out. The hospital has its own magazine, written, illustrated, and typed by the patients. Ex-patients are followed up and for those who live in the locality there is a weekly "club night" of entertainment, dancing, or lecture.

HYPERPYREXIAL HEAT-STROKE.

NOT long ago we commented on a number of papers on heat-stroke.[1] In their wake comes one from Australia, on Hyperpyrexial Heat-stroke, by K. G. Hearne.[2] This gives an excellent account of the climatic conditions which our troops had to contend with in Mesopotamia during the late war. The abnormal heat-wave—abnormal even for Mesopotamia—experienced in July, 1917, when for 18 consecutive days the maximum shade temperature averaged 119° F., provided a crop of hyperpyrexial cases which gave Dr. Hearne a valuable opportunity for clinical study. His experiences are recorded in detail, and while little fresh knowledge comes to light, much that has previously been conjectured receives ample confirmation. The chief interest of his paper lies in the success obtained in aborting threatened attacks. It is well proved that if suppression of sweating and frequency of micturition occurs, the sufferer should at once repair to the nearest sick-quarters for treatment. Dr. Hearne's experiences with hyperpyrexial attacks in troopships, and his deductions which rule out phlebotomus fever and malaria as primary causes of the condition, are decidedly helpful. It is perhaps a pity, however, that no mention is made of the presence or absence

[1] THE LANCET, Feb. 13th, p. 358.
[2] Med. Jour. of Australia, Feb. 13th, p. 226.

of indicanuria in his cases, for the discovery of indican would support the auto-intoxication theory which he dismisses as unlikely without confirmation. While it may be agreed that sweat suppression is a primary cause of heat hyperpyrexia, it is still quite probable that auto-intoxication plays a part.

CENTENARY OF C. J. HEWLETT AND SON, LTD.

WE have received a history of the house of C. J. Hewlett and Son, Ltd., put together from reports which have appeared in the pharmaceutical and scientific press, the occasion of the publication being the celebration this year of the centenary of the business. We have personal reasons for liking to think that the existence of a business for one hundred years is a proof not only of continuity but of progress.

The founder of the business, Mr. C. J. Hewlett, gained his knowledge of pharmacy by driving over England in a horse and gig as a commercial traveller for the now extinct firm of Tosswills. Between 1832 and 1870 he was associated with several partners in a business which was growing up on general lines, and in the latter year he was joined by his son, Mr. John Hewlett. The son struck out a special line by producing a number of high-grade non-secret pharmaceutical preparations, and establishing a large trade in them overseas. The founder of the firm died at the beginning of this century at the age of 90, and shortly afterwards the business was turned into a limited company, among the directors being his son, Mr. John Hewlett, his grandson, Mr. Vivian Hewlett, and Mr. J. D. Allman, the senior representative of the firm in the home markets. During the war the firm did excellent service in supplying drugs to hospitals, doctors, and pharmacists at home and abroad. Shortly afterwards Mr. John Hewlett, died, and was succeeded as chairman by his son, Mr. Vivian Hewlett, Mr. E. J. Millard being associated with him as managing director. Under their activities the firm has made great developments, material evidence of which is supplied by the extension of premises and the establishment, under Mr. Norman Millard, of an excellent analytical laboratory.

A centenary dinner will be held on Saturday April 23rd, at the Abercorn Rooms, Bishopsgate, E.C

ACID-BASE EQUILIBRIUM IN SKIN DISEASE

G. Milian and L. Brodier,[1] in a review of dermatological topics, quote some recent observations by Spillmann and Verain. Taking −7·35 as the normal pH, and using an electrometric method of determination, these workers find a definite acid-base disturbance in the blood of people suffering from eczema, eczematides, urticaria, prurigo, psoriasis, and dermatitis herpetiforme. They believe that this loss of equilibrium plays an important part in exudative affections, and eczema in particular. Twenty-two per cent. of the cases tended to the acid side, and 73 per cent. to the alkaline; there was considerable difference in the amount of variation from case to case, and apparently no relation to the severity of the clinical manifestations. It is of some value to note that in their experience a return towards normal in the acid-base balance is of good prognostic import, while persistence of the disturbance indicates the probability of a relapse. From the therapeutic point of view it is easier to rectify the acid tendency with sodium bicarbonate than to alter the alkaline tendency by means of phosphoric acid, calcium chloride in large doses, or autohæmotherapy. There is neither an "acid" nor an "alkaline" dermatosis. It is the loss of balance between the two which is of pathogenic importance, and often this is itself only a sign or effect of another disturbance, endocrine or vago-sympathetic. It follows that in the effort to counteract the ascertainable loss of acid-base balance, the physician must not shut his eyes to the possibilities of more fundamental factors.

[1] Paris Méd., 1932, No. 3, p. 45.

TOURS IN RUSSIA.

As announced in a letter in our issue of March 26th, the Society for Cultural Relations with the U.S.S.R. has arranged three tours in Russia, leaving London on July 16th, August 13th, and Sept. 10th. As these dates cut across those of the British Medical Association's centenary meeting in London (from July 21st) and the Physiological Society's meeting in Rome (August 29th), it has been decided to arrange an earlier tour if enough applications are received before May 20th.

The party would leave London on June 18th for a tour of Leningrad, Moscow, Nijni-Novgorod, and down the Volga to Stalingrad, returning to London by boat, and arriving on, or about, July 12th. The charge would be not more than £35 (inclusive of return fares, hotels, tips, food, theatres, and interpreters). Further particulars may be had from the secretary of the Society, 1, Montague-street, London.

MYASTHENIA GRAVIS.

"INQUIRER" writes: I would be very grateful to learn from any reader where to obtain some recent information concerning the ætiology and treatment of myasthenia gravis. The patient is a doctor.

Appointments

EDBROOKE, F. R., M.B., Ch.B. Brist., D.P.H., has been appointed Medical Officer of Health, Coulsdon, Purley, Beddington and Wallington Councils.

HOWIE, L. J., M.B., Ch.B. Edin., Asst. Medical Officer of Health and Asst. Tuberculosis Officer, Midlothian, West Lothian, and Peebles.

MCGARRITY, J., M.D. Edin., D.P.H., Medical Superintendent of the City Hospital, Little Bromwich, Birmingham.

TOPPING, M. D., Ch.B. Aberd., D.P.H., Medical Superintendent in the L.C.C. Public Health Dept.

Certifying Surgeons under the Factory and Workshop Acts: BRIGG, D. A., M.B., B.S. Lond. (Chipping Norton); CROSS, R. M. S., L.R.C.P. Lond., M.R.C.S. (Petersfield); and HAIR, A., L.R.C.P. Lond., M.R.C.S., D.P.H. (Prestcyn, Radnor).

Births, Marriages, and Deaths

BIRTHS.

HOWELL.—On April 7th, the wife of Dr. J. Bonnell Howell, Brook Green, W., of a daughter.

SMYTH.—On April 10th, at Wimpole-street, W., the wife of Michael Smyth, F.R.C.S., of a son.

MARRIAGES.

BIGBY—NEW.—On April 9th, at Southwark Cathedral, Dr. William Louis Murray Bigby to Hilda Marian, younger daughter of the late Mr. and Mrs. G. H. New, of Cheltenham.

HAMILL—FINDLATER.—On April 7th, at Our Lady of Victories, Kensington, John Molyneux Hamill, O.B.E., M.D., D.Sc., to Lesley, daughter of the late R. B. N. Findlater and Mrs. Findlater, of Queen's-gate, S.W.

DEATHS.

APPLETON.—On April 6th, at Canford Cliffs, Bournemouth, James Enderby Appleton, M.R.C.S., L.D.S. Eng., of Penticton, British Columbia, late of "Linda," Poole-road, Bournemouth.

BARTLETT.—On April 10th, at Burntwood-lane, Wandsworth, Edward Bartlett, M.R.C.S., L.R.C.P., L.D.S., late of Connaught-square, Hyde Park, and North Walsham, Norfolk, aged 87.

LAWSON.—On April 3rd, Richard Lawson, M.R.C.S., L.R.C.P., late of Balham Hill.

WADDY.—On April 8th, Henry Edward Waddy, M.R.C.S., L.R.C.P. D.P.H. Camb., of Rhossili, Brunswick-road, Gloucester.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

VICTORIA PARK HOSPITAL.—It was reported at the annual meeting last week of the City of London Hospital for Diseases of the Heart and Lungs, Victoria Park, E., that trade depression has reduced annual subscriptions and patients' contributions, while payments by county authorities in respect of treatment of their patients have also fallen off to a great extent because these bodies are increasingly building their own hospitals and sanatoriums.